ANNALS OF
INTERNAL MEDICINE

VOLUME 11 JUNE, 1938 NUMBER 12

ON MISTAKING OTHER DISEASES FOR ACUTE CORONARY THROMBOSIS *

By JAMES B. HERRICK, M.D., F.A.C.P., *Chicago, Illinois*

WHEN a previously misunderstood or overlooked disease has been shown to be common, when its symptoms are first described, for a time it is likely to be a front page medical news item. It is a best seller. A good illustration is afforded by appendicitis. The classic paper of Reginald Fitz in 1886 stirred surgeons and internists to a more accurate understanding of this condition, its frequency, diagnosis and—after some prolonged and lively discussion—its essentially surgical character from the standpoint of treatment. For a time there was a tendency to regard too readily nearly every acute pain in the abdomen as evidence of appendicitis. In the worthy effort not to call this disease something else, some other condition was often mistaken for appendicitis. Salpingitis, gall stones, renal or ureteral colic, purpura, twisted pedicles, small herniae, intestinal obstruction of various types were too often forgotten. And when subacute and chronic appendicitis swept into the medical ken, it was no uncommon thing for a patient suffering from constipation, or a spastic colon that had been abused by cathartics to be subjected to operation for supposed disease of the appendix. Indeed purely psychoneurotic states often deceived even the expert. So it has been with coronary occlusion.

In the earlier discussions that began about 20 years ago, attention was often drawn to the fact that formerly acute coronary obstruction had been called something else—ptomaine poisoning, acute indigestion, acute dilatation of the heart, acute heart failure, cerebral hemorrhage or thrombosis, or had been regarded as perforating duodenal or gastric ulcer, pancreatitis, disease of the gall-bladder, or other acute subdiaphragmatic emergency that is tersely—perhaps more graphically than grammatically—called "acute abdomen." There was need for warning against such error. This need has not lessened, in fact it has increased since it is now known that the accident may occur in relatively young individuals; that it may be ushered in by

* Read before the American College of Physicians, New York, N. Y., April 5, 1938.

symptoms less startling and less frank than those first described. Often only by critical study may one avoid this major diagnostic error. Wrongly to regard coronary thrombosis as something else may lead to unnecessary surgical operation, to faulty management, to embarrassing mistakes in prognosis. It may even be the cause of fatal results.

Today I wish to call attention to another aspect of this condition. There has developed a tendency in the other direction, viz., too readily to call some other disease coronary occlusion. This tendency is sometimes facetiously termed a fashion or fad, but it merits serious consideration.

In deprecating this tendency to regard too hastily any pain in the front of the chest attended by increase in the heart's rate or alteration of rhythm as indicative of heart disease and especially of a "heart attack," it would be unjust to give the impression that diagnosis of coronary disease is always easy, for it is not so. Nor should one lay all these errors to carelessness or ignorance on the part of the physician. Like the layman, he has become heart-conscious, perhaps even heart-panicky. He has a mental leaning towards coronary thrombosis due largely to his praiseworthy desire to guard his patient against the evil consequences of overlooking this life-threatening condition. Fortunately, the rest in bed that may be prescribed is generally harmless; it may be beneficial. Unfortunately, however, it sometimes deprives the patient of the benefits of timely surgical treatment or of a more suitable medical management. Unfortunately, too, it may aggravate an already existing psychoneurosis. We all know how deplorable is the condition of the one who has a firmly fixed fear concerning the heart.

This topic is presented not as something new, but as something that needs the emphasis of repetition. Others have written about it, as have I. I shall take the liberty of quoting, at times verbatim, from some of these papers of mine. My paper today will be little more than a recital, a cataloguing of conditions—some 30 altogether—that I have personally seen mistaken for acute coronary thrombosis. Some of these errors were my own. Cases of so-called chronic coronary occlusion—*oclusion lenta* of some of our South American colleagues—are not included. These offer a different, and also a difficult, problem.

Cardiac Conditions. Angina pectoris and coronary thrombosis are closely related pathologically. Thrombosis may be an incident, perhaps the culminating incident, in the history of frequently recurring angina of effort. It is not to be wondered at that they are easily confused. It is worthwhile, however, from the standpoint of prognosis and treatment to distinguish, if possible, between the pain brought on by effort, which disappears after quiet or the use of nitrites and the more enduring pain which may come on without provocative effort and which is attended by the well known shock, dyspnea, arrhythmia, fever, leukocytosis and altered electrocardiogram. The one condition speaks for a temporary relative ischemia of the cardiac muscle, the other for a more permanent ischemia. It is well to remember also that in some cases recurring attacks of angina are the

sequel of thrombosis. Also that angina of effort may cease after a coronary occlusion has converted the area of muscle that previously caused pain (when it was relatively ischemic on effort) into a scarred area practically dead, inert and painless.

Arrhythmias. Cardiac irregularities not dependent upon a coronary lesion may, especially in the neurotic, simulate acute coronary obstruction, particularly if they occur in suddenly developing paroxysms—extrasystoles, auricular fibrillation or flutter. More than once I have known a prolonged paroxysmal tachycardial attack to be taken for a coronary accident. The anxious sufferer, fearing death, may complain of pain; has a disturbed respiration. The skin may be grayish in color and bathed in sweat. The pulse disturbance may alarm both patient and doctor. A careful study showing absence of the more striking positive signs of an acutely damaged heart will usually enable one to assess these symptoms properly.

Neurosis. Frank cases of neurocirculatory asthenia may usually be easily recognized. In other instances the neurotic individual, perhaps upset by intimate association with a sufferer from distressing or fatal heart disease, or fed up on the stories of "heart attacks" in the health column of the daily paper, may present a puzzle difficult to solve. Some of the most satisfying results have been in convincing patients and doctors that there was no thrombosis, no organic coronary artery disease. Some of the most humiliating experiences have been when the subsequent history has shown that the supposedly functional symptoms were clearly on an anatomic basis. Especially perplexing are cases in which an individual who is "nervous" is found to have organic disease, such as duodenal ulcer or gall stones, and yet whose symptoms closely resemble those of the coronary artery syndrome, including at times an electrocardiogram that suggests myocardial damage. Does the duodenal ulcer, or the gall stone known to exist, cause all the symptoms? In the nervously hypersensitive patient do the conditions act as a trigger to set off an explosion resembling angina or acute thrombosis? Or has the patient both the abdominal and the thoracic disease? Careful, sometimes prolonged observation may be necessary before conclusion is reached.

Malingering. I have known malingerers to claim health insurance for feigned coronary accidents. Fraud of this kind may call for keenest diagnostic acumen, as well as for a Sherlock Holmes attitude in a study of motive and of character. On the other hand, I have seen several cases in which the suspicions of the insurance company that there was fraud were shown to be unwarranted. The later unimpeachable history, in some instances the sudden coronary death of the claimant, has shown that the arterial disease had been present.

Pericarditis. Pericarditis caused primarily by infection may in its symptoms and even its electrocardiogram closely resemble the pericarditis —generally aseptic—that often accompanies infarction. If careful search

be made, there may at times be detected possible primary infectious and infecting conditions, such as subacute rheumatic joints, tonsillitis, pneumonia, tuberculosis, etc. Help may also come from a more critical study of serial electrocardiograms in cases of pericarditis of various types. Barnes [1] in 1934 published a helpful paper dealing with electrocardiographic details. Paul Wood [2] says that in pericarditis with or without tamponade effects from effusions, there are changes in all three conventional leads with later negative T in all three, with unusually marked changes in Lead II. Wood calls this the T_2 type of electrocardiogram or the "pericardial T wave." These papers and others may be consulted for the pericarditic features of coronary occlusion.* The questions involved are of more than academic interest. Prognosis and treatment of the pericarditis would depend in large measure upon the underlying pathology of the condition.

Disease of the Aorta. The pain and distressed breathing together with changes in cardiac action due to syphilitic aortitis, with or without definite aneurysm, may be wrongly interpreted. So may the sudden severe pain of a dissecting aneurysm—which is usually in a non-syphilitic individual with hypertension—with its shock and frequently altered heart rate and rhythm. In the cases of dissecting aneurysm that I have seen the location of the pain in the back of the chest with roentgen-ray findings have been especially helpful in diagnosis. Rupture of the aorta into the pericardial sac, a not uncommon termination of dissecting aneurysm, may very strikingly resemble acute coronary thrombosis. In one instance my pride at having correctly diagnosed the dissecting aneurysm several weeks before took a heavy fall through the error of mistaking the terminal intrapericardial rupture for acute thrombosis.

Pulmonary Conditions. In this group were several cases of pleurisy, pneumonia, carcinoma of the bronchus. Massive collapse of the lung once due to carcinoma of a bronchus, in other instances following operations, has also been mistaken for acute coronary obstruction.

Three times acute pneumothorax was the cause of the error. In one ambulatory case the pneumothorax was partial, adhesions restricting the area of collapse to the upper left chest. In another case, a physician while dressing had a sudden pain in the left side of the chest, felt weak and nauseated, breathed with difficulty. He noticed that his pulse was rapid and small. He feared he had had a coronary accident. On careful physical examination, however, the heart was found displaced to the right. This with the altered signs over the lung on percussion and auscultation, and the roentgen-ray examination confirmed the diagnosis of ruptured lung. The

* Since reading this paper before the College I have seen the important article by Bellet and McMillan in the *Archives of Internal Medicine* for March 1938. This has a direct bearing on the topic under discussion. It offers an attractive explanation for the similarity of the electrocardiograms in various types of pericarditis and infarction viz. interference with the function of the myocardium. In infarction there is practical destruction of cardiac muscle. In pericarditis the function of the muscle is impaired by involvement by extension of the inflammation from the pericardium, with at times the added feature of pressure when there is a large pericardial effusion.

third patient, because of symptoms so closely resembling a coronary attack, had been kept in bed for many days. It was only by most detailed review of the history, careful physical examination including roentgen-ray of the chest and a critical study of the electrocardiogram, that it became clear that the accident had been an acute rupture of the lung. In none of these cases could tuberculosis be made out.

An embolus, at times perhaps a thrombus, in the pulmonary artery, unless the embolus be quite small, may cause symptoms that mimic in marvelous manner those so often seen in the fulminant type of acute coronary obstruction. The pain may be severe in the sternal or lateral region of the chest or in the epigastrium; it may go to the arms. Dyspnea is pronounced. There is shock, an ashy countenance, a drop in blood pressure. The pulse generally becomes rapid and small and may be irregular. The temperature may rise and the leukocytes be increased. No wonder one hesitates as to diagnosis. The history of an abdominal operation a few days before or the finding of signs of a thrombus in the superficial or deeper veins of the lower part of the body may be ground for suspicion. Or perhaps the patient has been confined to bed in the medical ward because of a broken down heart or some other chronic debilitating disease, bodily states that favor the development of thrombi in peripheral vessels or in the heart itself. The problem may be rendered still more intricate when one reflects that a pulmonary embolus with infarction may be the result of a coronary obstruction. An intracardiac thrombus that forms over the damaged myocardium may be—as when the septum is involved—in the right ventricle. Embolus from this source goes to the lung. This whole question, which deserves more extended consideration than can be given here, is discussed with much detail in Paul White's articles on cor pulmonale [3] and in the recent comprehensive paper of Barnes.[4] The important electrocardiographic features are there taken up.

Herpes Zoster. Herpes zoster is a prolific source of diagnostic error, at least until the skin lesion is in evidence or is brought into the evidence by being recognized. Three times I have seen herpes called acute coronary thrombosis.

Arthritis. I pass over with mere mention and no suggestions as to differentiation this very frequent cause of confusion. Changes in the costochondral articulations, the shoulder joints including the neighboring bursae, and spondylitis of the cervical and upper dorsal spine have often caused symptoms interpreted as due to disease of the coronary artery, either angina pectoris or thrombosis. Careful study of the history, examination of the joints as by roentgen-ray, the diagnostic use of heat, the negative electrocardiographic and cardiac findings usually enable one to reach a correct diagnosis. But perplexity is great when a patient has both arthritis and angina or a coronary occlusion and especially if such patient is neurotic.

Dr. Irons tells me of a case of fractured vertebra that had been diagnosed and treated as acute coronary thrombosis.

Abdominal Disease. As has often been remarked, acute coronary obstruction has many times been mistaken for an abdominal accident. The converse is true: symptoms due to abdominal conditions may simulate those of a cardiac accident. To remember this possibility and to decide definitely that the heart is to blame only when other causes such as gall stones, ulcer of duodenum or stomach, carcinoma, pancreatitis are excluded is usually all that is necessary. Decision may depend upon the presence or absence of characteristic earmarks of coronary disease—rapid heart, fibrillation, heart block, gallop rhythm, pulsus alternans, painful sensations in the neck, shoulder, arm or wrist. Electrocardiogram may be helpful, though one should not give too much weight, especially in the old, to variations that might be due to myocardial scars due to previous occlusions. At times with extremely puzzling but clearly serious symptoms, exploratory operation may be justifiable. Acute gastritis may confuse. Spastic colon may have acute manifestations that are misleading. Then there is eventration of the diaphragm. In one such case only the most painstaking physical and roentgen-ray examination made it possible to exclude primary heart disease.

Hernia of the diaphragm may be a stumbling block. A doctor who said he had had a "growling gall-bladder" with occasional colicky attacks, came to me much alarmed by what he and a colleague felt sure was an angina with a coronary occlusion. I satisfied myself by the dye test that there was no evidence of a pathologic gall-bladder. Evidence of damage to the heart was lacking. On fluoroscoping the stomach there was found a diaphragmatic hernia that would hold perhaps two ounces. Even then the doctor was not convinced, nor is he now after more than two years.

I have seen a tabetic with gastric crisis in whom there was a question as to a coronary accident. There was no proof that such had occurred.

Diabetes. Coronary thrombi are not unusual in diabetics who are prone to have arteriosclerosis. One has to be wary, however, in diagnosing an acute obstruction in a diabetic, even though he have chest pain, dyspnea, quite sudden symptoms of collapse with faltering pulse and drop in blood pressure. Oncoming coma may quite closely simulate a coronary attack. On the other hand, one must not too hastily diagnose chronic unrecognized diabetes in a patient who has an acute thrombosis, for sugar in the urine is not unusual in patients suffering from this accident.

My conclusion is simple: it is easy to mistake other diseases for coronary thrombosis. This is a statement that none would have denied before hearing the paper. Then why should I write or talk about it? Is it not true that some of our most embarrassing and costly errors are due to the fact that, for the moment, we forget things that we know full well? That in looking for the unusual we overlook the obvious? Merely to think of the other disease is often to avoid the error.

The object of this paper, then, has been not to present something new, but to repeat something of value that is old—lest we forget.

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INFARCTION OF THE HEART

II. SYMPTOMATOLOGY OF ACUTE ATTACK*

By WILLIAM BENNETT BEAN, M.D., *Cincinnati, Ohio*

IN the first part of this study the conditions underlying and precipitating cardiac infarction were analyzed. In this paper the symptomatology of the acute attack and related data will be presented.

INCIDENCE

Statistical reports [8, 7] show that coronary artery disease is today much more prevalent than as recently as 20 years ago. The records of this hospital for the first and second halves of the 31-year period investigated are summarized in table 1. It is improbable that the increased percentage of

TABLE I
Incidence

	1906–1921	1922–1936
Hospital admissions	215,164	443,913
Deaths	23,234	32,077
Autopsies	2,439	7,187
Clinical diagnoses of cardiac infarction; corrected by adding undiagnosed autopsy findings, and subtracting mistaken diagnoses		1,287
Known dead after admission attack		748 (58 %)
Autopsies in which infarcts were found *	23 (0.9 %)	277 (3.9 %)

* The first adequately described protocol of myocardial infarction appeared in the records for 1873, the first year for which records are available. Clinical data on significant factors are lacking so the early cases were not used in the analysis.

TABLE II
Incidence by Five-Year Periods

Period	Total Autopsies	Number of Infarcts	Per Cent
1906–11 (6 years)	1,100	13	1.2
1912–16	701	5	0.7
1917–21	638	5	0.8
1922–26	1,417	36	2.5
1927–31	2,181	67	3.1
1932–36	3,589	174	4.9
Total	9,626	300	3.1

* Received for publication September 10, 1937.
From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

autopsies or the interest in infarction accounts for the increase in cases. Nevertheless, one need not postulate that fundamental factors in pathogenesis have become more severe but rather assume that they are active in more individuals for longer periods of time.[8]

Groups of Cases

For convenience in analysis the cases were divided into three groups: (1) 114 cases in which death occurred within six weeks. These were single infarctions with the exception of five cases with two infarctions during that period. (2) 75 cases with old and recent infarcts which survived the initial lesion by six weeks or more. (3) 111 cases with old scars, usually single but occasionally multiple.* When a scar or infarct was found at autopsy and a reliable clinical history was available, it was often possible to determine the date of acute infarction in retrospect, even when it had been overlooked during life. There were cases, however, where the symptoms were so trivial as to have been disregarded, or where the syndrome of gradual congestive failure progressed without episode and no date for acute infarction could be established.

Diagnosis

Table 3 gives the data on correct diagnosis in acute attacks since 1922, when the first verified clinical diagnosis was made in this hospital. An illuminating point is the rarity with which the condition was diagnosed un-

Table III

Diagnosis with Reference to Pain in Acute Attacks

Period	Acute Cases Examined	Correctly Diagnosed	Per Cent	Cases with Pain	Percentage of Correct Diagnosis in Which Pain Was Present
1922–26	25	9	36	9	100
1927–31	35	21	60	19	90
1932–36	116	84	72	76	90
	176	114	65	104	91

less pain was present. During the last five years about three-fourths of the acute cases were correctly diagnosed. In painless cases the diagnosis (when correct) was usually made on electrocardiographic evidence.

A commentary on diffusion of knowledge regarding the syndrome of painful infarction is the frequency with which this diagnosis is now uncritically made when, in fact, some other disease is responsible for the symptoms. Warnings of this trend have recently appeared in papers by Averbuck,[3] Barker, Wilson and Coller,[4] Weiss,[45] Herrick [23] and Bishop.[5] With

* There were seven cases with three infarcts, four with four and two who had several scars and five acute episodes.

this point in mind the records were examined in all autopsied cases in which the clinical diagnosis had been made. It was found that in 26 cases an unqualified diagnosis of coronary thrombosis, occlusion or infarct, and in 52 cases a tentative diagnosis, was recorded where the lesion was not found at autopsy. The conditions obtaining in this group of cases are summarized in table 4. In 37 cases anginal pain had been present. The lungs and

TABLE IV

Conditions Mistakenly Diagnosed Coronary Thrombosis

	Provisional Diagnosis	Unqualified Diagnosis	Total
Hypertension, coronary arteriosclerosis no infarct ("angina pectoris, status anginosus")	20	9	29
Pulmonary embolism	4	5	9
"Heart negative; no anatomical cause of death"	4	5	9
Dissecting aneurysm of aorta	4	2	6
Lobar pneumonia	2	3	5
Bronchopneumonia	2	—	2
Cholecystitis and cholelithiasis	2	—	2
Rupture of aortic cusp; bacterial endocarditis	2	—	2
Syphilitic aortitis, narrow coronary orifice and angina pectoris	2	—	2
Pernicious anemia and angina pectoris	1	1	2
Peritonitis	2	—	2
Perforated peptic ulcer	1	—	1
Infarct of kidney	1	—	1
Infarct of spleen	1	—	1
Infarct of mesentery	1	—	1
Carcinoma with metastasis to heart	1	—	1
Acute purulent pericarditis	—	1	1
Rheumatic heart disease	1	—	1
Epidural abscess	1	—	1
Total	52	26	78

Additional conditions reported in the literature not demonstrated in this series: cervical arthritis, neuralgia, neurosis, herpes zoster, spontaneous pneumothorax, interstitial emphysema, carcinoma of the stomach, acute pancreatitis, appendicitis, diabetic acidosis, esophageal hiatus hernia, paroxysmal tachycardia, luetic aneurysm, and massive embolus to the heart.

pleurae were involved in 16. In eight some acute condition in the upper abdomen was the source of confusion. Six of the cases were dissecting aneurysms. In nine there was " no anatomical cause of death."

Many of the cases included in this list were moribund or in desperate condition when admitted; examination was meager and the diagnosis was manifestly a guess. In other cases important factors were overlooked. It is obvious that the great majority of these mistakes in diagnosis were due to misinterpretation of symptomatic pain, just as the large proportion of missed cases of infarction were those in which pain was not noted. Doubtless cases of sudden syncopal death were also included. Additional conditions mistakenly called coronary thrombosis, reported in the literature, are included in table 4.

Status Before Infarction

Table 5 lists the symptoms in 125 cases with reliable history of the period prior to initial infarction. *Left ventricular failure,* as manifest by orthopnea and cardiac asthma, was present in about one-third. Peripheral edema indicating *right ventricular failure* was also present in about one-third. There were few cases in which isolated failure of either ventricle continued for any appreciable length of time. Usually, however, dyspnea and orthopnea appeared before peripheral edema. Previously existing failure was much less frequent in those surviving the first attack than in those succumbing. The average age at initial infarction in those with previous failure was 62.2 years, as against 61 years for the entire group. Sex, hypertension and other predisposing factors were similar in the groups with and without failure before infarction.

Table V

Symptoms Prior to Initial Infarct (125 Cases)

		Number of Cases	Percentage
1.	Dyspnea on exertion	88	70
2.	Weakness	67	54
3.	Cough	51	41
4.	Nocturia	50	40
5.	Orthopnea	47	38
6.	Ankle edema	44	35
7.	Angina pectoris	42	34
8.	"Indigestion"	35	28
9.	Paroxysmal nocturnal dyspnea	30	24
10.	Palpitation	30	24
11.	Syncope, fainting spells	28	22
12.	Users of digitalis	18	14
13.	Hemiplegia	11	9
14.	Users of nitroglycerin	9	7
15.	Auricular fibrillation	2	2

Weakness was an antecedent complaint of about half of the cases. It was usually a manifestation or interpretation of congestive failure, but in a few indicated associated noncardiac disease. *Hypertension* had been observed before infarction or was demonstrated afterward in about 50 per cent. There was no unusual aspect of its symptomatology except for the greater frequency of anginal pain. *Cough* was noted in 41 per cent. *Nocturia,* a complaint of 40 per cent, was in many due to a local complication (prostate, bladder) but in some was of diabetic or cardiorenal origin.

Medical literature reveals no uniform agreement regarding the association of *anginal pain* and congestive failure in coronary disease. Wearn [42] and Keefer and Resnik [24] stress the tendency of angina of effort to disappear upon development of congestive failure. On the other hand, Willius and Brown,[50] Bruenn [7] and Master [31] observed a larger proportion of cases where the two occurred simultaneously. In this series exactly half of the cases with anginal pain had previous congestive failure. In a few others

angina had declined with the accession of failure. The fact that many patients with severe manifestations of cardiac disability were not prevented from exercising to the point of inducing anginal pain is in part evidence of their profound disregard for the inconvenience of dyspnea and edema.

Disturbances of gastrointestinal function were frequent, as indicated by anorexia, flatus, belching or constipation. In some these symptoms were associated with chronic alcoholism, in others with gall-bladder disease, but in the majority they were associated with passive congestion of the viscera.

Palpitation occurred in a fourth of the cases. It was probably related to extrasystoles or to some factor other than *auricular fibrillation*, which was present in only two cases before infarction. This is in marked contrast to the frequent appearance of fibrillation following infarction.

There were 28 cases in which some type of *syncope* had been present. Sufficient data were not present in these patients reliably to evaluate the nature of these attacks.

TABLE VI

Signs and Symptoms

	First Attack			Second Attack			Total Per-centage
	Number	Data	Per Cent	Number	Data	Per Cent	
1. Dyspnea	108	114	95	67	70	96	95
2. Enlarged heart	72	87	83	53	62	85	84
3. Weak heart sounds	77	91	85	56	68	82	84
4. Râles	91	109	83	54	66	82	83
5. Cyanosis	69	90	77	44	51	86	80
6. Cough	32	46	70	27	32	84	76
7. Pallor	38	55	69	26	33	79	73
8. Pain	104	138	75	40	61	66	72
9. Orthopnea	66	97	68	37	59	63	66
10. Sweating	31	52	60	15	25	60	60
11. Vomiting	47	80	59	16	27	59	59
12. Ankle edema	58	105	55	32	59	54	55
13. "Shock"	79	138	57	34	75	45	53
14. Restlessness	50	114	44	37	75	49	46
15. Tachycardia (rate over 100)	43	103	42	32	67	48	44
16. Systolic murmur	38	99	38	24	62	39	39
17. Cheyne-Stokes respiration	25	104	24	25	35	71	36
18. Ascites	11	42	26	14	33	42	33
19. Cloudy sensorium	41	156	26	16	49	33	28
20. Enlarged liver	11	60	18	7	31	23	20
21. Gallop rhythm	12	100	12	16	60	27	18
22. Prodromal phenomena	28	135	21	2	51	4	16
23. Bradycardia (rate below 80)	16	103	16	10	67	15	15
24. Angor animi	17	140	12	8	40	20	14
25. Pericardial friction rub	17	112	15	7	64	11	14
26. Pulsus alternans	10	106	9	6	42	14	11
27. Precordial hyperesthesia	8	100	8	3	38	8	8
28. Jaundice	6	100	6	5	51	10	7
29. Anuria	8	189	4	→			4
30. Hiccough	4	189	2	→			2
31. Uremia	3	189	2	→			2

Prodromal Period

In spite of the fact that the suddenness of the attack in cardiac infarction is considered characteristic,[18] Kahn [17] and Feil [12] have observed that many patients who have painful infarction experience anticipatory symptoms of varying types. Frequently there is a mild anginal pain, burning in quality, with or without radiation, not necessarily related to effort and often differing qualitatively from the angina of effort. Feil suggested that this pain may arise from the gradual formation of a thrombus. In this series of cases there were several patients with prodromal symptoms whose infarction was dependent on sclerotic narrowing of the artery without intermediation of a thrombus. In some patients, therefore, symptoms arise merely during formation of the infarct from disturbances of muscular physiology. Others, without warning, suddenly had their pain in all its intensity. Painful prodromal symptoms appeared 28 times. They were observed only twice before second infarcts and in no subsequent ones.

Symptomatology of Acute Attacks

Though a few adequate descriptions of the symptom complex of coronary thrombosis with cardiac infarction antedated Herrick's classic contribution,[21] it has been only within the last two decades that the symptomatology has become widely known. Notable among the clinical descriptions are those of Hamman [18] and Levine.[25] There are still some considerations which can be established by a statistical study, in spite of a liability to err in attempting rigidly to classify sensations.

Sensorium. Interpretation of symptoms varies with the clarity of perception in the individual patient. In a quarter of the cases there was some clouding of the sensorium. It occurred with vascular collapse or in the end stages of congestive failure, also in association with hemiplegia and aphasia, with alcoholism, with diabetic coma and with acute infections. Such cases with questionable data were not included in the various tables.

Dyspnea. Subjective difficulty in breathing was the most frequent symptom in the acute cases. Where its absence was noted it may have been present before the patient was observed. The sensation of difficulty in breathing early in an attack was often associated with a feeling of constriction. In a few cases apprehension was a factor. The difficulty in breathing subsequent to the infarction is regarded as a symptom of left ventricular failure,[43] as indeed it may be in cases where failure antedates infarction. In this series the hydrothorax found at autopsy undoubtedly added a terminal burden. Table 7, which records respiratory rate, shows the great frequency of *tachypnea.* It was usually, but by no means invariably, associated with dyspnea. The respiratory rate was found to have increased by ten or more per minute four times as frequently as a similar decrease was found. In rare cases hyperventilation seems to have occurred.

Vital capacity determinations were made in relatively few of the cases;

TABLE VII
Respiratory Rate in Fatal Attacks

Rate per Minute	First Attack		Second Attack		Totals	
	Initial	Terminal	Initial	Terminal	Initial	Terminal
16–20	36	18	15	15	51	33
21–25	39	29	23	20	62	49
26–30	27	34	15	13	42	47
31–35	4	13	8	9	12	22
36–40	5	12	5	6	10	18
41+	4	9	5	8	9	17
	115	115	71	71	186	186
Increase of 10 or more	28		10		38	
Decrease of 10 or more	5		5		10	

these showed a reduction from the normal. Whenever several measurements were recorded a decrease was observed. *Cheyne-Stokes' respiration* was observed in one-quarter of the initial attacks and three-quarters of the subsequent ones. *Orthopnea* was a very frequent finding associated with other evidence of advanced failure. In a few cases it was the heralding symptom of infarction.

Left ventricular failure was further indicated by pulmonary *râles* in 83 per cent of the cases. Acute pulmonary edema was also a frequent finding. There were many cases of terminal bronchopneumonia.

Cyanosis was present both in cases in which "shock" predominated and in those in which congestive failure was prominent. In three-fourths of the cases it was combined with pallor to produce the "leaden tint spread over an earthy hue of skin," a prominent feature of the typical facies.

Cough frequently appeared with an acute episode of infarction, or changed its character when it had been present before. Acute and chronic bronchitis, pneumonia, pulmonary infarcts and congestion could not account for the cough in all cases.

Pain, though the most dramatic symptom of infarction, was recorded in no more than 72 per cent of the acute attacks. Recent literature contains numerous reports of painless cases.[9, 10, 37, 40] In this series special effort was made to find reasons for the presence or absence of pain. Orthopnea, ankle edema or breathlessness at rest had been present in approximately half of the cases having painful first attacks and in almost two-thirds of those having painful second attacks (table 8). Pain and congestive failure were no more mutually exclusive in acute attacks than were angina and failure in the period before infarction. No individual who had suffered anginal pain prior to initial infarction failed to have pain with the acute attack, so far as the circumstances are known. Only two of 13 patients who had pain with effort after recovery from the initial infarction

TABLE VIII

Occurrence of Failure Prior to Infarction in Patients Having Pain in Acute Attacks

Attack	No Cardiac Symptoms Before	Dyspnea on Exertion	Orthopnea, Edema or Dyspnea at Rest
First	33	6	36
Second	14	5	9
Third	0	0	6
Total	47	11	51

failed to have pain with the second attack. One of these had sudden increase in failure, the other weakness and syncope.

It may be of some significance that among the Negroes and Hebrews, of whom there were 16 each, only three Negroes had a history of cardiac pain and only seven had pain with infarction. On the other hand, 11 of 12 Hebrews had had angina and 14 (all with data) had painful acute attacks. This is compatible with the ideas of varying sensitivity to pain in different individuals brought forward by Libman.[27] No other clinical factors in this series could be correlated with pain. Three distinct groups of cases appeared: (1) those having angina and painful infarction; (2) those having painful infarction without previous angina; (3) those having no pain at any time before, during or after the acute episode.

TABLE IX

Relation of Symptoms to Arterial Lesions

	L. A. D.	R. M.	L. Cir.	L. A. D.; Cir.	R. M.; L. M.	L. M.	L. A. D. L. Cir. R. M.	Total
No radiation	49	7	3	2	3	4	2	70
Left arm	13	1	4	3		2		23
Both arms	8	1		1	1		2	13
Both arms and both shoulders	4	2	1	1				8
Left arm and shoulder	5	1		2				8
Both shoulders	2					1		3
Left arm and both shoulders	3							3
Right chest	2	1						3
Right arm	1	1						2
Left shoulder	1		1					2
Angle of left scapula	1		1					2
Right shoulder	1							1
Left arm and jaw					1			1
Neck and jaw					1			1
Neck				1				1
Both arms and jaw	1							1
Both arms and back				1				1
Back	1							1
	92	14	10	11	6	7	4	144
Cases having no pain with acute attack	37	4	1	3				45

Original Site of Pain

Substernal, 88; epigastric, 29; precordial, 21; left shoulder, 5; back, 1.

Table 9 shows the location of arteries involved in cases with pain, with or without radiation, and in cases without pain. While certain trends appear, it is quite clear that location of arterial change and infarction are not the only determining elements in the occurrence of pain or its radiation. This is in agreement with the observations of Bruenn and his associates.[7] Herrick [22] suggests that absence of pain with acute infarction may depend upon the occurrence of thrombosis which renders the area absolutely ischemic, nerves and muscle becoming functionless at the same time. Sutton [41] believes that in such cases where pain occurs anastomoses suffice to make the ischemia only relative. In painful attacks after infarction Eckerson et al.[11] believe scar tissue may cause the pain. An alternative idea is that arteries with mechanically reduced lumens cannot adequately supply blood through new collateral channels if the basal flow is already maximal when one of the arteries becomes obstructed.

The fact that pain had occurred in many cases where rapidly developing infarction followed structural narrowing of an artery *without thrombosis* demonstrates that thrombosis of an artery per se is not necessary to produce pain in cases of infarction. It indicates that pain arises from some change in the muscle even though mediated chiefly by periarterial nerves. There was no constant relation of pain to any type of infarct as far as could be judged from the description of infarcts in the protocols.

TABLE X

Radiation of Pain in Two Attacks

First Attack			Second Attack		
Artery	Site of Pain	Radiation	Artery	Site of Pain	Radiation
1. Left anterior descending	Substernal	None	Left anterior descending	Substernal	None
2. Left anterior descending	Substernal	None	Left anterior descending	Substernal	None
3. Left anterior descending	Substernal	None	Left anterior descending	Substernal	None
4. Left anterior descending	Substernal	Left shoulder	Left anterior descending	Substernal	None
5. Left anterior descending	Substernal	None	Left anterior descending	Substernal	Left arm
6. Left anterior descending	Substernal	None	Left anterior descending	Substernal	Left arm
7. Left anterior descending	Substernal	Left arm	Left anterior descending	Substernal	None
8. Left anterior descending	Substernal	None	Right main	Substernal	Both arms
9. Left anterior descending	Substernal	None	Right main	Substernal	None
10. Left circumflex	Substernal	Both arms and shoulders	Left anterior descending	Substernal	Both arms and shoulders
11. Right main	Substernal	Left arm and shoulder	Left anterior descending	Substernal	Left arm and shoulder
12. Left circumflex	Substernal	None	Right main	Substernal	None

A recent article has appeared in which the suggestion was made that the radiation of pain to the left depends on primary overburdening of the left ventricle, no matter where the arterial damage.[30] For this reason cases are tabulated in which accurate clinical study was made in two painful attacks, and in which the arteries involved were ascertained (table 10). It is difficult to explain the clinical manifestations of these cases on a topographical or structural basis. Attempts to predict the absence or presence of pain from the description of the infarct resulted in a large proportion of failures. The inevitable conclusion is that factors producing pain and governing its location and radiation in infarction do not leave any pathognomonic stamp on the heart.

A feature related to both pain and dyspnea is the *sense of constriction,* crushing or pressure which was so frequently found in these cases. Table 11, with description of characteristics of pain, indicates its frequency in

TABLE XI

Types of Pain

	Number of Cases
Crushing pressure	44
Squeezing, constricting, vice-like	29
Choking, smothering, suffocating	18
Sharp, stabbing, knife-like	11
Sore, aching, dull	11
"Excruciating"	7
Burning	5

association with pain, and it was also found in certain cases without pain. Mackenzie [29] considered it to be a manifestation of actual spasm of the intercostal muscles induced reflexly. The sensation is analogous to that which a normal individual experiences when he "has his wind knocked out" following a blow, usually to the body or head, not sufficient to induce syncope. Such a sensation is also comparable to that occurring in nightmares. One is unable to breathe satisfactorily in spite of intense effort and struggling. Its exact physiologic nature has not been demonstrated.

In the cases where pain was not present in the acute attack, several varieties of the so-called *substitution symptoms* indicated infarction. These are listed in table 12. The most frequent examples were cases with sudden dyspnea or signs of rapidly developing left ventricular failure, as stressed by Wearn.[42] In a smaller group the prominent findings were referable to the central nervous system, such as weakness, syncope, nervousness or dizziness, which Weiss [44] has emphasized.

Sweating as a symptom of infarction is of two kinds. The first is part of the picture of shock and collapse, usually appearing early.[46] The other occurs later and is a manifestation of protein disintegration, along with fever and leukocytosis.[19] It may be so severe as to produce dangerous loss

TABLE XII

So-Called Substitution Symptoms

	Number of Cases
1. Sudden onset of cardiac asthma, orthopnea, or pulmonary edema	11
2. Gradual increase in congestive failure, no acute episode	9
3. Sudden increase in severity of preëxisting failure	6
4. Weakness and syncope	4
5. Sudden onset of dyspnea and edema	4
6. Sudden onset of suffocation and choking	2
7. Sudden onset of palpitation (auricular fibrillation present)	2
8. Vomiting, dizziness, and dyspnea	2
9. Angor animi and cardiac asthma	1
10. Dyspnea, weakness, and nervousness	1
11. Dyspnea, weakness, and syncope	1
12. Severe weakness and increase in failure	1
13. Weakness and dizziness	1
14. "Paralysis" of left arm, paresthesia, no pain	1

of body fluids and chlorides. Sweating was noted in 60 per cent of these cases.

Nausea and Vomiting. Vomiting was observed in 59 per cent of acute episodes, contrary to White's [48] finding. It was usually associated with pain and shock, though it appeared in cases where neither was present. Fourteen cases had received morphine before vomiting, and in two overdigitalization was probably the cause. In most of the cases it seemed to be a reflex phenomenon similar to sweating, set off by the strong medullary bombardment of impulses from the heart. This is the explanation given by Hatcher and Weiss [20] over ten years ago.

Restlessness. In contrast to the victim of a bout of angina, a patient with painful infarction soon observes that activity or posture is powerless to relieve pain. As a consequence all gradations from moderate uneasiness to maniacal thrashing and writhing may be found. Some form of restlessness was observed in nearly half of the cases. This purposeless activity is familiar to any one who has experienced severe pain. A few cases had a strange apprehensive restlessness even when no pain was present.

Angor Animi. The nature of the sensation of impending death has been investigated particularly by English writers, notably Gowers and Allbutt. Recently Ryle [34] advanced the explanation that such a sensation arises from organic or functional disturbances in the medulla. It may occur in cases of dissecting aneurysm, according to McGeachy.[28] It has been observed after transient dyspnea following the injection of sodium cyanide in circulation tests.[47] Angor animi should not be confused with the rational conviction that death is imminent, nor the desire for death expressed at times by those suffering excruciating agony. Angor animi was noted in 22 cases: 17 times in the first attack, eight times in the second (four times in both first and second) and once in the third. Apparently the phenomenon depends on the mental and emotional status of the individual rather than

upon the morphology of the cardiac disturbance. Recently Wortis,[51] in discussing the cardiac psychoses, concluded that "anxiety is a body state and can be provoked by physical disease." Though this symptom was noted in a few cases during the course of the illness no case was diagnosed *cardiac psychosis.*

Hiccough, a symptom sometimes seen in posterior infarct associated with diaphragmatic irritation,[47] was observed in only four cases, and one of these had uremia. A few instances of *abdominal distention* appeared where no organic lesion was found to cause it. *Diarrhea* was recorded in several. *Anuria,* present in a few of the rapidly fatal cases, was not specifically noted in any case surviving as long as a week.

The symptoms in the first and second attacks are compared in table 6. The most striking differences are the increased severity of congestive failure in the second attack and a decrease in frequency of pain. Some relationships of pain and failure in two attacks are tabulated in tables 8 and 13 and the occurrence of anginal pain in relation to painful attacks is noted.

TABLE XIII

Characteristics of Onset of Second Attack

	Those with pain in first attack	No pain with first attack	First attack not known; had history of angina
Failure and pain	10	7	2
Failure	7		
Pain	6	4	4
Angina and pain	1	1	
Cardiac asthma	1	5	
Angina, failure, and pain	3		
Syncope, etc.	4	3	1
Smothering	1		

Relation of Angina and First Painful Infarction

	Number of Cases
No angina but pain with first attack	23
Anginal pain before; none following attack	8
Anginal pain before and after	4
No anginal pain before but present after	13

PHYSICAL EXAMINATION

The various findings determined by examination of the *heart* are presented in table 14. *Tachycardia* was present in the majority of cases throughout the period of observation, though in an appreciable number there was no elevation of rate. In fatal cases an increase of heart rate was observed twice as frequently as a corresponding decrease, but in the individual case was not of prognostic value. There were three cases of bradycardia, one of which had complete block.

TABLE XIV
Examination of Heart

		First Attack	Second Attack	Total
Size	Enlarged	72	53	125
	Normal	15	9	24
Sounds	Poor, weak, distant	77	56	133
	Good	14	12	26
Murmurs	Systolic	38	24	62
	Diastolic	13	2	15
	None	61	38	99
Gallop		12	16	28
Rhythm	Regular	60	53	113
	Auricular fibrillation	22	13	35
	Extrasystoles	23	5	28
	Flutter	2	0	2
Friction Rub		17	7	24
Rate	Below 60	1	2	3
	61–80	15	8	23
	81–100	44	25	69
	101–120	30	20	50
	121–140	11	8	19
	141 +	2	4	6
Rate rose 10 or more during illness		23	16	39
Rate fell 10 or more during illness		9	11	20

Eighty-three per cent of cases were considered by the examiner to have *enlarged hearts.* No constant standard or linear measure of the size was recorded, but the clinical impression was verified in many instances by roentgen-ray findings and in the others at autopsy. *Heart sounds* were described as weak, distant or muffled in almost the same proportion of the total cases. The loudness of sounds was inversely related to the degree of shock in most instances. In addition, myocardial failure may be associated with feeble heart sounds. It has been shown experimentally by Wiggers [49] and in man by Scott and his associates [36] that the involved area of the ventricle rapidly ceases motion upon acute infarction.

Though a *systolic murmur* is frequently found in cases of infarction, it is of no diagnostic significance unless it is known to have been absent before. The diastolic murmurs were dependent upon valvular disease in most cases. *Gallop rhythm,* another manifestation of an overburdened heart, was recorded in surprisingly few cases. *Auricular fibrillation* was evident clinically many more times than it was actually demonstrated by electrocardiogram, which indicates the transient nature of this arrhythmia in many cases. *Extrasystoles* were often observed; they were probably most frequently of ventricular origin. No striking differences were noted in the heart examinations made in first and second attacks.

In spite of the fact that *pericardial friction rubs* were observed by several clinicians during the last century, their significance was not widely understood until the last two decades. Gorham [16] and Gordinier [15] stressed the finding as a valuable diagnostic confirmation. In several reported series varying proportions of cases with friction rubs are recorded. In 21 per cent of the groups listed in table 15 friction rubs were heard. In the

TABLE XV

Pericardial Friction Rub

Examined in Acute Attacks	Sterile Pericarditis at Autopsy	Rub Heard
176	58	24 (14 per cent)

Time After Infarction Rub Was First Heard

	6 hours	12 hours	Days 2	3	4	5	6	7	Second week	Time not known
Number of Cases	1	2	2	4	2	0	1	1	4	7

Clinical Evidence of Pericarditis

Author	Number of Cases Examination Acute Attack	Number of Cases with Friction Rub	Percentage
Gorham	6	5	83
Gordinier	13	11	85
Wearn	19	2	11
Wolff and White	23	3	13
Longcope	16	0	0
Hamman	10	1	10
Blumer	109	32	29
This Series	176	24	14
	372	78	21

present series fresh pericarditis was found at autopsy 58 times and a rub had been heard in 24 cases, or 41 per cent. Cases of purulent pericarditis and uremia were discarded. It is certain that friction rubs are frequently missed, but in a few cases plastic pericarditis may cause adhesions sufficient to prevent rubs. In addition the infarcted area does not contract actively, as do normal parts of the ventricle. In one case a rub from pericarditis of the posterior wall was heard. Another case had had a rub but 10 days later, when death occurred, no evidence of pericarditis remained. The rub was first heard in many cases on the second, third or fourth day. For this series 80 per cent of all cases with pericarditis had mural thrombi. Such a combination indicates that the infarction extends through the entire thickness of the ventricular wall. It is not certain that mural thrombi would be present in as large a proportion of non-fatal cases with pericarditis.

Arterial Blood Pressure. Since actual blood pressure readings were not

recorded in most individuals for the period before the initial attack, information is available only for the time from infarction until death. Table 16 gives data for the highest blood pressure reading during the first few days

TABLE XVI

Highest Blood Pressure Following Acute Attacks

Systolic

Diastolic	200+	175–200	150–175	125–150	100–125	75–100	0–75	0
100+	9	14	14	8	3			
75–100	1	2	5	12(19)	2(19)	(5)		
50–75	1		1	3(7)	3(15)	3(12)		
0–50						(7)	(2)	
0								(2)

Pulse Pressure

Pulse Pressure	10	20	30	40	50	60	70	80	90	100	125	150
Number of Cases	1(1)	5(15)	3(18)	8(13)	16(14)	16(15)	11(3)	6(1)	3	2	4	1

( ) = non-hypertensive.

TABLE XVII

Laboratory Findings

	First Attack			Second Attack			Per Cent
	Number	Data	Per Cent	Number	Data	Per Cent	
Unqualified E.K.G. Diagnosis	49	56	88	28	39	72	81
Leukocytosis above 10,000	66	84	79	37	47	79	79
Fever	60	86	70	40	57	70	70
Albuminuria	56	98	57	30	57	53	55
N.P.N. above 40	21	68	31	18	44	41	35
W.B.C. in urine	25	75	33	17	44	39	35
Casts in urine	11	61	18	15	42	36	25
Transient glycosuria	11	96	11	4	50	8	10

after the attack. In spite of the fact that these patients ultimately died, many were able to maintain a high level of pressure for a few days. Uncontrolled factors, such as changes in degree of failure, bed rest, diuresis, make detailed analysis of cases of little value. Among the groups into which cases fell were (1) those with a rise in tension during the acute attack, especially cases with pain and restlessness [14]; (2) those whose tension fell rapidly but later, if they survived, recovered partially; (3) those who maintained a previously established hypertension without significant fall early in the course; (4) those who had no marked change from normal before or after. The group with falling tension was the largest.

TABLE XVIII

Highest Oral Temperature

	Degrees Fahrenheit	First Attack	Second Attack	Total
Subnormal	Below 96	5	4	9
Normal		21	13	34
	98–99	13	15	28
	100	25	16	41
	101	14	6	20
	102	8	3	11
		86	57	143

Day of Highest Fever

Day	First Attack	Second Attack	Total
1	1	4	5
2	8	5	13
3	5	3	8
4	7	2	9
5	5	2	7
6	4	0	4
	30	16	46

Fever. An elevation of temperature is a frequent finding in sterile infarction. Levine[25] has emphasized the fact that oral temperature determination is not reliable. Many cases with no fever had a large degree of shock and dyspnea which interfered with satisfactory observation of mouth temperature. Cases with acute infections were not included in the analysis but cases with varying degrees of congestive failure were used, although it is acknowledged that this complication alone can produce fever.[38] In this series fever was observed in only 70 per cent of the attacks, reached a peak most often from the second to fifth days in initial attacks, but earlier in the second attacks. It lasted an average of four days in uncomplicated cases. In no case could fever above 102° F. be attributed to an uncomplicated cardiac infarct. In general the larger infarcts gave rise to higher and more sustained fever. Terminal rises in temperature were usually found in patients dying primarily of congestive failure, infarcts of the lung or pneumonia. It was found that fever and leukocytosis appeared together in 72 cases, leukocytosis without fever in 29 cases and fever alone in 15 cases.

LABORATORY STUDIES

Leukocytosis. The leukocytosis that follows infarction of the heart was emphasized first by Libman.[26] This characteristic finding was absent in one-fifth of these cases seen in the acute attacks, although repeated examinations were not made in all instances. The cases without early complications

had increased white cell counts, as listed in table 19. It was found that where serial counts had been made the highest leukocytosis appeared most frequently on the second or third day, though in a few cases observations

TABLE XIX

Leukocytosis

White Blood Cells in Thousands	First Attack	Second Attack	Total
Below 10	18	10	28
10–12	23	7	30
12–14	12	6	18
14–16	13	6	19
16–18	8	6	14
18–20	4	5	9
20–25	4	5	9
25–30	1		1
30–35			0
35–40	1	2	3
	84	47	131

Average of those with leukocytosis 15,500

Day of Highest Leukocytosis
Cases with 2 or more counts

Day	1	2	3	4	5	6
Number of Cases	1	10	14	6	3	7

were not made on the first day. There was an invariable preponderance of polymorphonuclear neutrophiles, ranging from 63 to 93 per cent. Filament-nonfilament differentiation was not made. In a few cases a second rise in the white blood cells was associated with evidence of spread of the infarct, though such a rise usually signified pulmonary infarction, bronchopneumonia or embolic accident.

Electrocardiographic Studies. An exhaustive analysis of electrocardiograms in this series is precluded by lack of space. A summary of the findings is contained in table 20. A normal sinus rhythm was found in about two-fifths of the cases; sinoauricular tachycardia was frequent. More cases were found to have ventricular extrasystoles than auricular fibrillation, though the latter was found clinically as a transient phenomenon in many cases in which it was not recorded electrocardiographically.

In a clinical series of 328 cases of coronary thrombosis, Salcedo-Salgar and White [35] found 13.1 per cent with heart block (auriculoventricular 3.6 per cent, intraventricular 8.9 per cent and both 0.6 per cent). In sharp contrast are the figures in this series which reveal a P–R interval of 0.20 second or more in 30 per cent of the cases and an intraventricular conduction defect with Q–R–S interval of 0.10 second or longer in 52 per cent of the

TABLE XX

Electrocardiographic Data

	First Attack (56 cases)	Second Attack (39 cases)	Old Scars (35 cases)	Total 130
Rhythm				
Normal sinus	28	20	6	54
Auricular fibrillation	6 (2 transient)	3 (1 transient)	7	16
Auricular flutter	2		3	5
Auricular extrasystoles	1		3	4
Sino-auricular tachycardia	10	4	6	20
Paroxysmal auricular tachycardia	2	2		4
Sino-auricular standstill and escape			3	3
A. V. dissociation	2	2	2	6
Ventricular extrasystoles	7	6	5	18
Paroxysmal ventricular tachycardia		2		2
P–R interval				
to .15	23	14	17	54
.16–.19	20	13	10	43
.20–.23	9	10	5	24
.24+	4	2	3	9
Q–R–S interval				
to .09	29	19	18	56
.10–.13	20	13	12	45
.14+	7	7	1	15
Low amplitude	22	10	12	44
Ventricular preponderance				
Left	30	23	19	72
Normal	22	11	15	47
Right	4	5	2	11
Diagnosis				
Coronary disease	13	9	6	28
Anterior infarct	15	8		22
Posterior infarct	18	8	1	27
Not localized infarct	3	3		6
Digitalis T-waves	3		2	5
Bigeminy	2		1	3

cases. This indicates that on the average such conduction defects are of grave prognostic import. When conduction defects were correlated with lesions involving primarily the right or left coronary artery, striking results were obtained (table 21). When the main lesion was in the right coronary artery, 42 per cent had a P–R interval of at least 0.20 second, while only 20 per cent of those with lesions of the left arterial tree had such changes. Q–R–S intervals longer than 0.10 second were observed in 73 per cent of those with right artery damage and only 41 per cent of those with left artery damage. This difference is dependent upon the source of the blood supply to the impulse-producing areas, since it is claimed that the right artery supplies the A–V node in 90 per cent of hearts and the S–A node in 70 per cent. Clinically described auricular fibrillation was equally frequent with both types of lesion.

The electrical axis was found to show left-sided preponderance in 60 per cent of cases; no deviation was found in 31 per cent of the cases; 9 per cent showed right axis deviation. Nine of the 11 cases of right-sided pre-

TABLE XXI

Conduction Defects

	Site of Main Arterial Lesion		Total
	Left	Right	
P–R interval			
below 0.16	31	6	37
0.16–0.19	24	9	33
0.20–0.23	11	8	19
0.24+	3 (20%)	3 (42%)	6 (26%)
	69	26	95
Q–R–S interval			
below 0.10	41	7	48
0.10–0.13	22	11	33
0.14+	6 (41%)	8 (73%)	14 (49%)
	69	26	95
Auricular fibrillation (clinical)	43	11	54

ponderance, however, showed intraventricular conduction defects. Low voltage (5 mm.) electrocardiograms were found in 34 per cent of the cases.

A differential diagnosis between anterior and posterior infarction was not always made, especially in early cases or those complicated by intraventricular conduction defects or bizarre tachycardias. When localization was ventured, especially after the use of the chest lead, it was found that all diagnoses of anterior infarcts were correct, with the exception of one which was lateral and posterior. Of the 26 designated posterior, six were not correct, three being anterior and lateral left ventricle, one anterior and apex of both ventricles, and two anterior base of left ventricle. In every case where Q_5 was absent an anterior infarct was present, though a small Q_5 was found in three cases of anterior infarct. When a large Q_5 was found the lesion was invariably posterior or posterior and lateral left ventricle.

Blood Non-Protein Nitrogen. The association of non-renal uremia with congestive failure was observed by Forster in 1915.[13] Recently Steinberg[39] has expressed his belief that a high or rising non-protein nitrogen is an ill omen in prognosis after coronary thrombosis. Since in this series it was impossible to estimate kidney function before the infarct, or to separate primary cardiac from primary renal failure, all cases with data were included in analysis. The level of blood non-protein nitrogen is found in

table 22. In 73 cases there was no appreciable deviation from normal during the course of the illness; in 11 cases it rose an average of 17 mg. per cent; and in seven it fell an average of 34 mg. per cent. Approximately one-third of the cases had elevated levels of blood non-protein nitrogen, but neither the level nor the direction of change was a valid individual prognostic indicator in this series.

TABLE XXII

Non-Protein Nitrogen of Blood

Mg. Per Cent	First Attack	Second Attack	Total
20–30	26	9	35
31–40	21	17	38
41–50	8	6	14
51–60	9	6	15
61–70	0	0	0
71–80	1	3	4
81–100	1	2	3
101–150	2	1	3
	68	44	112

Sedimentation Rate. Rabinowitz [33] believes the sedimentation rate is a valuable prognostic sign after infarction. In this series, although it was uniformly increased when determined in acute attacks, some of the patients died and others recovered. Rapid sedimentation rate has value as a non-specific sign of many conditions (large cardiac infarct, pulmonary embolism, infection) which decrease the likelihood of recovery.

Urinary Findings. The urine presents no characteristic picture after infarction of the heart. Abnormal findings depend on preëxisting or concomitant states. Albuminuria, frequently transient, appeared in more than half of the cases. It was associated most often with chronic vascular nephritis or chronic passive congestion of the kidneys. Gross infarction of the kidney occurred 28 times with characteristic urinary changes when the acute episode was observed. Kidney or bladder infection was noted 11 times. Anuria, first observed by Hamman,[18] was present in several patients who died within the first two days. No case could be found where a fall in blood pressure after infarction could be blamed for subsequent uremia. The urinary findings are summarized in table 23.

A *transient glycosuria,* first noted by Levine [25] has been studied recently by Raab and Rabinowitz [32] and Blake.[6] The condition may be related to the transient glycosuria observed after cerebral vascular accidents, which Aring and Merritt [2] believe is not conditioned by the type or location of the lesion. Raab and Rabinowitz believe it is caused by a disturbance of the vegetative centers in the brain which govern carbohydrate metabolism. It was detected in 15 of 146 cases where routine urine examinations were made. It appeared in only 2 patients without pain and in only five without

evidence of shock. There was no relation to age, sex, hypertension, fever, failure or angor animi. One patient had a transient glycosuria with his initial attack but none in a second, 19 months later, which is taken to in-

TABLE XXIII
Urinary Findings

	First Attack			Second Attack			Percentage Both Attacks
	Positive Cases	Number with Data	Per Cent	Positive Cases	Number with Data	Per Cent	
Albuminuria	56	98	57	30	57	53	55
White cells	25	75	33	17	44	39	35
Casts	11	61	18	15	42	36	25
Transient glycosuria	11	96	11	4	50	8	10

dicate that it does not necessarily represent a pre-diabetic state nor an anatomical change in the pancreas.

SUMMARY

1. The incidence of cases of cardiac infarction coming to autopsy increased fourfold in the later of two 15-year periods investigated.

2. Of 300 cases in which autopsy was done, 114 died within six weeks of the initial infarction; 75 cases had multiple lesions and survived more than six weeks; old scars were found in 111 cases.

3. Correct diagnosis was rare in the absence of pain. Mistaken diagnosis was usually confused by the symptom of pain.

4. One-third of the cases showed signs of congestive failure before acute infarction.

5. A prodromal period of pain occurred in 16 per cent of acute attacks.

6. Pain and congestive failure occurred together in many cases. Dyspnea was the most frequent symptom, and where associated with a sense of constriction merged into the ill-defined domain of pain.

7. No constant morphological finding could account for the vagaries of pain, its presence or absence, its location and radiation. Some evidence indicated it to be conditioned by individual differences, a cerebral rather than cardiac function.

8. In acute cases without pain the onset was frequently characterized by sudden accession of failure, less often by central nervous symptoms (syncope, weakness).

9. Tachycardia, enlarged heart, feeble heart sounds and arrhythmias were frequently encountered.

10. Pericardial friction rubs were heard in 41 per cent of cases with acute pericarditis.

11. The arterial blood pressure was found to remain elevated in a large number of cases, though the majority showed declining levels.

12. Fever and leukocytosis, although usually present, were absent in an appreciable number of cases.

13. Electrocardiographic studies revealed prolonged P–R interval in 25 per cent and prolonged Q–R–S intervals in 46 per cent of all cases. These conduction defects were almost twice as common in predominantly right artery involvement as in left. The diagnosis of anterior infarction was usually correct, but one-fifth of those diagnosed posterior infarcts were wrongly localized. A large Q-apex invariably indicated posterior location and absent Q-apex invariably indicated anterior infarction.

The urinary findings were found to be nonspecific.

The author wishes to express his appreciation and gratitude to Dr. Soma Weiss for his help and kindness in this study.

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ELECTROCARDIOGRAPHIC STUDIES IN CLINICAL AND EXPERIMENTAL PULMONARY EMBOLIZATION *

By William S. Love, Jr., M.D., F.A.C.P., G. W. Brugler, M.D.† and Nathan Winslow, M.D.‡, *Baltimore, Maryland*

In 1935, McGinn and White [1] reported certain aberrations in the electrocardiograms derived from five patients suffering with pulmonary embolization. These deviations from normal were as follows:

1. Prominent S-wave and low origin of the T-wave in Lead I, the ST segment starting slightly below the baseline.
2. Staircase ascent of the ST segment from the S-wave to the T-wave in Lead II.
3. The presence of Q_3, and inversion of the T-wave in this lead.
4. T-waves of opposite sign to normal in the precordial lead.

They considered it probable that the electrocardiographic changes consequent on pulmonary embolism were due to dilatation and partial failure of the chambers of the right side of the heart.

Scherf and Schonbrunner [2] report eight cases diagnosed clinically as pulmonary infarction in which electrocardiograms were made. In one case there was ST_1 depression, T_1 inversion, and elevation of ST_2 and ST_3; in another, elevation of ST_1 with depression of ST_2 and ST_3. A third case exhibited elevation of ST_1 and depression of ST_2 and ST_3. Two further cases presented depression of both ST_1 and ST_2; in only one were the changes similar to those described by McGinn and White. The remaining cases had flattened T-waves in Leads I and II.

Hazzard and Palmer [3] reported a single instance with electrocardiographic study. The ST segments are perhaps slightly depressed in Lead I, and T_2 and T_3 are inverted. In the first tracing made on this patient T_4 is upright, and the rest of the tracing conforms to what would be expected in a Wolferth Lead IV. Subsequent tracings show a reversal of direction of all deflections in the fourth lead without other noteworthy change, suggesting that the precordial electrodes had been reversed.

Love and Brugler [4] reported seven cases of pulmonary embolization, of which five showed consequent electrocardiographic aberrations and two did not. They found the common deviations from normal to be depression of the ST segments in Leads I and II, or in II alone, together with changes of the coronary type in Lead III, and a reversal of the direction of the T-waves in the precordial lead. Q_3 was, at times, present. Since the above report

* Received for publication February 23, 1938.
From the Department of Medicine, University of Maryland.
† Hitchcock Fellow in Medicine, School of Medicine, University of Maryland.
‡ Deceased.

we have obtained electrocardiographic studies subsequent to pulmonary embolism, on five more patients. Of these five, three revealed no significant changes in the electrocardiogram. Two presented ST segment depression in Leads I and II, and flattening of T_2. In one, ST_3 was also slightly depressed. Both showed T_3 inversion, one T_4 notching, and one T_4 of opposite sign to normal. Figure 1 presents the tracings obtained from a colored male, aged 40, (*a*) immediately following pulmonary embolism; (*b*) one week later; (*c*) following a second embolism of the lung; and (*d*) after recovery, one month subsequent to the second attack. Note the return of the electrocardiogram to normal configuration in the last tracing. Thus, of 12 cases of pulmonary embolism or thrombosis observed by two of us, five showed no consequent electrocardiographic aberration, and seven did.

In our opinion, the significant electrocardiographic changes noted in these cases are depression of the ST segments in Leads I and II, flattening, but rarely inversion, of the T-waves in Lead II, at times an abnormal Q_3, and usually T_3 inversion. The T-waves were abnormal in the precordial lead in five of the seven cases showing electrocardiographic changes. They were of opposite sign to normal in four.

The present study is an attempt to determine whether such electrocardiographic changes following pulmonary embolization can be produced experimentally in animals, and, if so, to discover their cause.

A number of investigations has already been made upon experimental pulmonary embolization. We shall quote only those which are more or less related to the problems studied by us. It is stated that from 50 per cent to 85 per cent of the pulmonary circulation must be obstructed before marked changes take place.[5, 7, 8, 9] It has been noted that dilatation of the right ventricle is usually striking.[8, 9, 10, 11] The pulmonic arterial pressure rises,[5, 11, 12] venous pressure rises,[12, 13] and arterial pressure falls.[7, 12, 13]

Comparatively few observations have been made on the effect of experimental pulmonary embolization upon the electrocardiogram. Krumbhaar[14] reported in 1934 the results obtained in 1916 with experimental obstruction of the pulmonary artery. He noted increase in size of the P-waves, abnormal ventricular deflections, at times right axis deviation, deep S_1, and Q_2, and suggested that it was possible that these aberrations in the QRS waves were due to bundle branch block. He noted further that the T-waves sometimes became enlarged, and sometimes, inverted or diphasic. Otto[15] reported exaggeration of normal T-wave negativity. The tracings following artificial pulmonary embolization, published by Mosler,[16] show extrasystoles, diminished voltage of QRS and T-waves, ventricular escape followed by supraventricular tachycardia and depressed ST segments, and culminate in heart block and ventricular fibrillation. Anderson,[17] after experimental pulmonary embolization, observed tachycardia and disturbances of the ST segments and inversion of the T-waves. The coronary T was stated by him to have been encountered only once. Katz and Buchbinder,[8] after dissemination of mercury in the pulmonary circuit, did not

find right axis deviation even after marked dilatation of the right heart, but did observe aberrations in the ventricular complexes and T-wave changes. Frommel,[18] cited by McGinn and White, found sino-auricular tachycardia, auriculo-ventricular dissociation, auricular flutter and fibrillation and ventricular flutter and fibrillation.

It has been suggested that the cardiac disturbances following clinical or experimental pulmonary embolization may be due to circulatory deficiency of the coronary arteries as a result of obstruction to the blood flow,[16, 8] or as a result of vagal effects upon the coronary flow,[2] or as a result of the fall in aortic pressure.[19, 5] McGinn and White [1] have attributed these effects to acute dilatation of the right heart and have introduced the term "acute cor pulmonale." Love and Brugler [4] stated that the parts played by mechanical obstruction to the pulmonary circulation, anoxemia of the heart muscle, reflex changes in the coronary circulation, and the preëxisting state of the coronary arteries should be taken into consideration.

Methods of Study

All experiments were carried out upon average-sized dogs. Ether anesthesia was used in most animals, with a respiration machine in those in which the chest was opened. Intravenous nembutal was used in a few animals. For the purpose of producing pulmonary emboli mineral oil was injected into the jugular vein in one animal. As we might have expected, widespread oil embolism resulted, and this experiment is not included in our report. Liquefied petrolatum jelly was tried, but promptly solidified in the jugular vein, and was successfully made use of in only one experiment. Granulated agar in normal salt suspension was tried in three experiments, but because of difficulties of injection into the jugular vein, was not used further. We finally used most successfully clotted blood from the animal experimented upon, colored with India ink so that the resulting pulmonary emboli could be readily discerned.

As preliminary experiments, and in order to determine for ourselves the electrocardiographic effects of experimental coronary occlusion, ten animals were subjected to ligation of the anterior coronary rami, the posterior coronary rami, or all available coronary supply. The results of these experiments in general agree with the results obtained by others.[20, 21] As a rule, but not always, anterior ligations produced the Lead I type of coronary curves; posterior ligations always produced the Lead III type coronary curve. We would stress, in view of what we will report, that all of these experiments resulted in the elevation of the ST segments in one or more leads. T-waves are not always immediately inverted. The ST segment deviation occurs within a few minutes of the ligation, and relaxation of the ligature usually results in a prompt return to the norm for that animal. In two experiments, ligation of all available coronary supply resulted in elevation in all leads (figure 6). It may be noted in passing that auricular and ventricular extrasystoles, auriculoventricular dissociation, and idioventricular rhythms, including ventricular tachycardia and fibrillation, occurred not infrequently when the ligatures were maintained in position for some time.

It may be stated at once that following the pulmonary embolization experiments, and following partial obstruction of the pulmonary artery, electrocardiographic changes quite similar to those noted in human cases of pulmonary embolism and thrombosis were obtained. In order to determine the cause of these changes, the following types of experiments were performed:

(1) To determine what rôle, if any, the condition of shock played in altering the electrocardiogram, four dogs were rather rapidly bled to exsanguination. This experiment also gives some evidence on the rôle of acute anemia in producing electrocardiographic changes.

(2) To determine if previous coronary injury, in itself of insufficient degree to produce electrocardiographic changes, would do so when associated with a condition causing shock, ligatures were placed about the anterior descending branch of the left coronary, tightened until apparent changes were noted by observing the movements of the string as they were being recorded, then loosened until the galvanometer movements had apparently returned to normal, and then the animal was slowly bled to death.

(3) To determine what electrocardiographic changes are consequent on experimental pulmonary embolization, such embolization was produced by injecting into the jugular vein granulated agar suspended in normal salt solution, in three experiments, and clotted blood from that animal, colored with India ink, in 10 experiments. (No difference was noted in the results obtained by these two methods of producing artificial pulmonary embolism.)

(4) To ascertain if there were any differences in the results of obstruction of the pulmonary circulation in the lung vascular bed and obstruction caused by mechanical narrowing of the pulmonary artery, ligatures were so placed about the artery that an estimated narrowing of the lumen of this vessel of more than 50 per cent was obtained.

(5) Whether or not any effect of the preceding types of obstruction or embolization is mediated through the vagus or sympathetic nerves was determined by a series of experiments in which the vagal and sympathetic cords were interrupted. The vagi were separated from the vagal-sympathetic cords and interrupted in the neck; ramisection and ganglionectomy of the thoracic sympathetic nerves plus severing the post-ganglionic fibers in the neck were performed in one experiment, and in two, the sympathetics were interrupted in the neck only. In several experiments both vagi and sympathetics were interrupted.

(6) Tracings obtained following embolization or pulmonary artery ligation were compared with those obtained in myocardial ischemia due to partial or complete coronary ligation, with those obtained in ischemia due to hemorrhage, and with one obtained subsequent to asphyxia in an otherwise normal dog.

General Comments

It has been commented upon many times that the direction of the T-waves is quite inconsistent in dogs. Our observations bear this out. More commonly they were inverted in Lead I and upright in Leads II and III. It has also been noted that many experimental procedures performed upon the dog may produce T-waves of opposite sign to that which they formerly exhibited. We noted especially in those cases where the chest was opened that alteration in the direction of the T-wave not infrequently accompanied this procedure. Therefore, although we have accepted for normal the tracing obtained after the chest was opened, we do not stress T-wave variations. On the other hand, we have observed no variation in the ST segments following such procedures and we do attach importance to alterations in this portion of the electrocardiographic curve in the experiments performed. We have not been primarily interested in the arrhythmias that have occurred in embolization or ligation of the pulmonary artery, but will state at this point that extrasystoles—more commonly of ventricular origin—were not infrequent; that sinus bradycardia was observed five times; that tracings similar to bundle-branch block occurred four times; auricular flutter, once; auriculoventricular dissociation, four times; idioventricular tachycardia, twice; and ventricular fibrillation, six times. Right axis deviation occurred in one experiment only. Minor changes in the QRS complexes were common.

Six animals survived the experiment, and four of them were then sacrificed and autopsied. Two were allowed to live following embolization experiments, but died the following night. All animals were autopsied and all showed considerable degrees of right-heart dilatation. In nine animals diffuse plugging of the small vessels was noted, and in six, in addition to some diffuse plugging, masses of thrombotic material were found in the larger pulmonary arteries. Identical electrocardiograms were obtained in either form of embolization.

In two such experiments venous and arterial pressures were graphically recorded. It was confirmed that a significant fall in arterial pressure and a rise in venous pressure occurred as a result of artificial pulmonary embolism.

Mosler [16] comments that vagal section inhibits the tachypnea following pulmonary embolization. In all of our experiments, tachypnea was a prominent feature, and we also noted that this reflex was abolished by vagal section.

I. The Effect of Shock Produced by Hemorrhage

Four dogs were bled to death. Only the changes noted in dying hearts were observed: sinus tachycardia, sinus bradycardia, varying degrees of heart-block, ventricular tachycardia, and ventricular fibrillation. No changes in the ST segments or T-waves were noted.

Following the opening of the thorax in our experimental animals—an extensive operation which might well be considered shocking—T-wave changes were frequent. However, we stress the point that the ST segments were not affected by this.

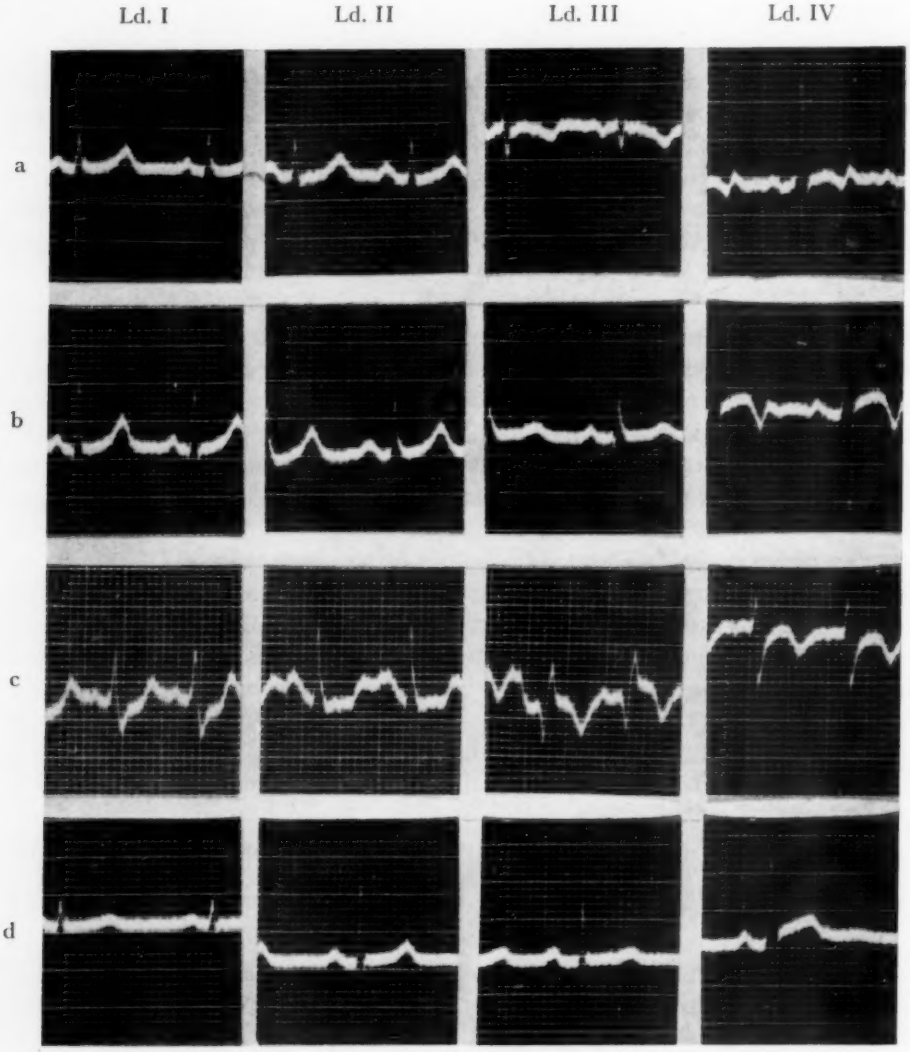

FIG. 1. Electrocardiograms obtained from clinical case of pulmonary embolism.

(*a*) 24 hours after onset. Note arching of ST_3 and ST_4, T_3 inversion, and initial inversion of T_4.

(*b*) One week after *a*. Note alteration in direction of QRS_3. T_3 has become upright, and T_4 more sharply inverted.

(*c*) 35 days after first tracing pulmonary embolism occurred again. Note S_1, marked depression of the ST segments in Leads I and II, and elevation of ST_3. A Q_3 has appeared, and T_3 and T_4 are deeply inverted.

(*d*) This tracing was obtained one month after *c*. The patient had completely recovered. The electrocardiogram has returned to normal.

(Chest leads taken with right arm electrode posterior, left anterior.)

We obtained electrocardiograms on a number of clinical cases suffering from shock produced by such diverse factors as hemorrhage at child-birth, extensive major surgery, gunshot wounds of the chest or abdomen, automobile accidents, etc. · Tachycardia and low-voltage QRS waves were commonly noted. No significant deviation in the ST segments or T-waves were observed in any case.

II. Shock Plus Preëxisting Coronary Injury as a Factor in Electrocardiographic Abnormalities (Figure 2).

A ligature was placed around the anterior descending branch of the left coronary artery, and this ligature was tightened until electrocardiographic aberrations appeared. The ligature was then partially released until the curve had apparently returned to normal. The animals were bled, and further tracings taken. Table 1 summarizes the effects upon the ST segments and T-waves caused by these procedures. In one animal the ligature was partially applied and not removed. In this experiment ST_1, within 10 minutes, became somewhat elevated. ST_2 and ST_3 became convexly arched, and T_3, inverted. After bleeding, QRS_3 became entirely negative, ST_2 and ST_3 took off far below the base line, and the T-waves were large and upright. ST_1 was elevated.

Table I

Effect of Anterior Coronary Ligation and Subsequent Bleeding upon the ST Segments and T-Waves of the Electrocardiograms of Dogs

	Dog No. 2		Dog No. 4		Dog No. 6	
	ST	T	ST	T	ST	T
Normal tracing	Ld. I baseline Ld. II baseline Ld. III baseline	flat − −	baseline baseline baseline	flat − −	baseline baseline baseline	flat − −
After ligation	Ld. I baseline Ld. II elevated Ld. III elevated	flat + +	baseline elevated elevated	flat + +	elevated depressed depressed	flat − −
Release of ligature	Ld. I baseline Ld. II baseline Ld. III baseline	flat + +	baseline baseline baseline	flat + +	baseline baseline baseline	flat − −
After bleeding	Ld. I baseline Ld. II markedly elevated Ld. III markedly elevated	flat + +	baseline depressed depressed	flat ++ ++	baseline elevated elevated	flat − −

These findings indicate that, if previous coronary damage be present, hemorrhage may alter the electrocardiogram, and that then the ST segments usually behave as in coronary occlusion.

A woman, aged 48, developed profound shock and died, two days following an abdominal operation. The electrocardiogram obtained several

hours before death was typical of a Lead II and III coronary curve. At autopsy there was no evidence of pulmonary embolization and no evidence of coronary thrombosis. There was a moderately advanced arteriosclerosis of all of the larger branches of the left coronary artery. No electrocardiogram had been obtained prior to operation. There had been slight dyspnea on exertion during the preceding year. We are not justified in drawing conclusions from this case, since we do not know what the electrocardiogram was before the operation. However, in view of the experiments re-

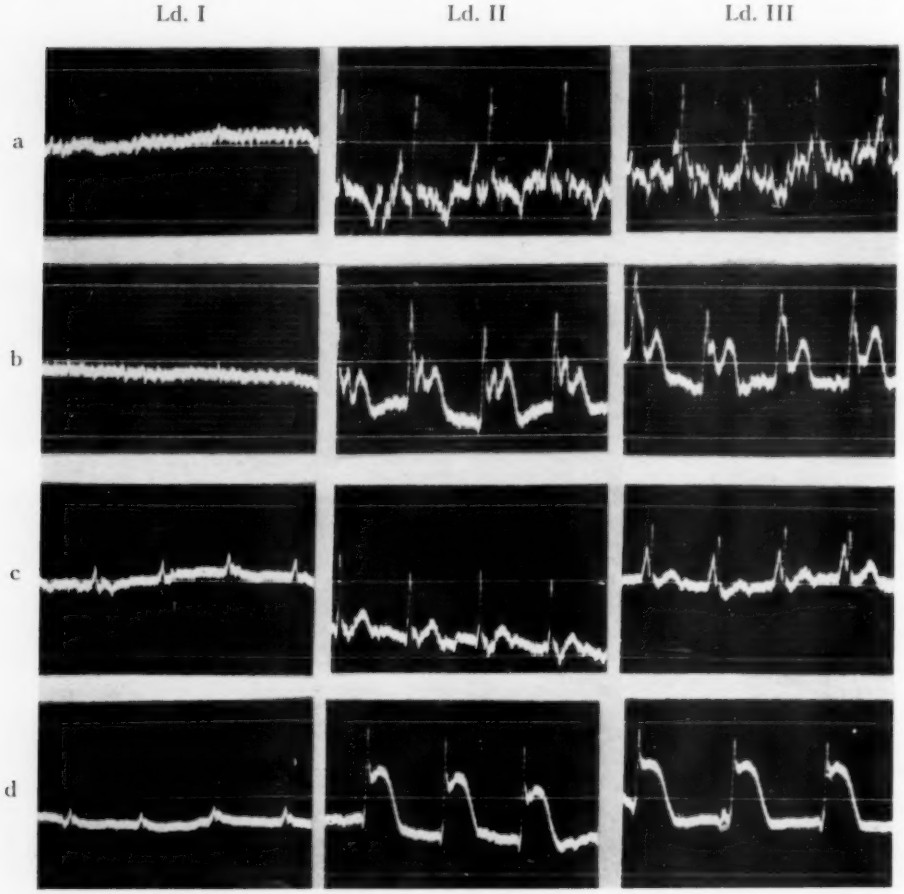

FIG. 2. Partial coronary ligation and hemorrhage experiment.

(*a*) Electrocardiogram obtained from anesthetized dog after opening chest.

(*b*) Tracing obtained practically immediately after ligation of anterior descending branch of left coronary. ST segments in Leads II and III become markedly elevated and the T-waves in these leads become large and upright.

(*c*) The ligature was then partially loosened and tracing taken 30 minutes after *b*. Note return of ST segments to baseline. The T-waves, however, remain upright.

(*d*) Tracing taken 15 minutes after *c*. The animal had now been bled copiously with ligature as in *c*. Note that ST segments in Leads II and III are again markedly elevated. This type of curve could not be produced by hemorrhage alone.

In *b*, *c*, *d*, an arrhythmia is present.

ported above, it seems quite possible that the diminution in coronary circulation attendant upon shock, plus the presence of coronary arteriosclerosis, may produce an electrocardiogram strongly suggestive of coronary occlusion. We wish to reiterate that, with only one exception, the electrocardiographic changes noted in this type of experiment and in this clinical case are similar to those following upon coronary occlusion, especially as regards elevation of the ST segments in one or more leads.

It should be possible to verify clinically these observations by recording the electrocardiograms in a series of elderly patients about to undergo major operations and then to repeat such examinations in those who may become shocked. A certain number of such cases would undoubtedly come to autopsy, when the state of the coronary vessels could be observed.

III. Electrocardiographic Changes Noted Subsequent to Experimental Pulmonary Embolization (Figure 3)

Experimental embolization was produced, as outlined above, in 13 dogs. Of these, two died almost immediately while the first tracing was being taken, and both showed intraventricular conduction defects similar to those noted in bundle-branch block. At autopsy these two animals were found to have such massive plugging of the large pulmonary arteries that one could assume practically complete obstruction of the pulmonary circuit to be present.

In two more animals a continuous record was made of Lead II. Progressive depression of the ST segment below the base line was the only finding of significance. In the remaining nine animals the most striking changes were noted in the ST segments, depression below the base line in one or more leads being present in all. This depression occurred in Lead I alone in one instance, in Leads I and II in three instances, in Leads II and III in two, and in Lead III alone in two. One animal died before a record could be secured.

Significant changes in the T-waves in the standard leads occurred in six experiments. In five of these the direction of the wave was changed from upright to inverted, and this change was noted in Lead II once, in Leads II and III once, in Lead III twice, and in all three leads once. In one animal the T-waves of Leads II and III became much more deeply inverted than they had been before embolization. Precordial-left-leg leads were secured in five animals. In one no significant changes occurred in this lead; in another the ST segments remained at the base line but the T-waves were altered; and in three ST_5 became distinctly elevated. T_5 remained unchanged in one experiment, became more deeply inverted once, and altered its direction twice—from upright to inverted once, and from inverted to upright once.

One would conclude from these experiments that the most consistent electrocardiographic finding following experimental pulmonary embolization is a depression of the ST segments in one or more leads, Lead II being,

by far, the one most commonly involved. These findings are entirely consistent with the ST aberrations noted in clinical cases of pulmonary embolization. In the fifth lead the ST segment became elevated in three of five experiments. As has been seen, changes in the direction of the T-wave are not uncommon in experimental embolization, and in the standard leads these occurred most commonly in Lead III, and in only one experiment in Lead I. These observations are also consistent with clinical cases of pulmonary embolism and infarction. As regards the precordial lead, T-wave reversal occurred in three of five experiments.

IV. Effects of Mechanical Obstruction of the Pulmonary Artery upon the Electrocardiogram (Figures 4, 5)

With the chest opened, the left pulmonary artery was ligated in one experiment, and later the main artery was constricted. In four more animals,

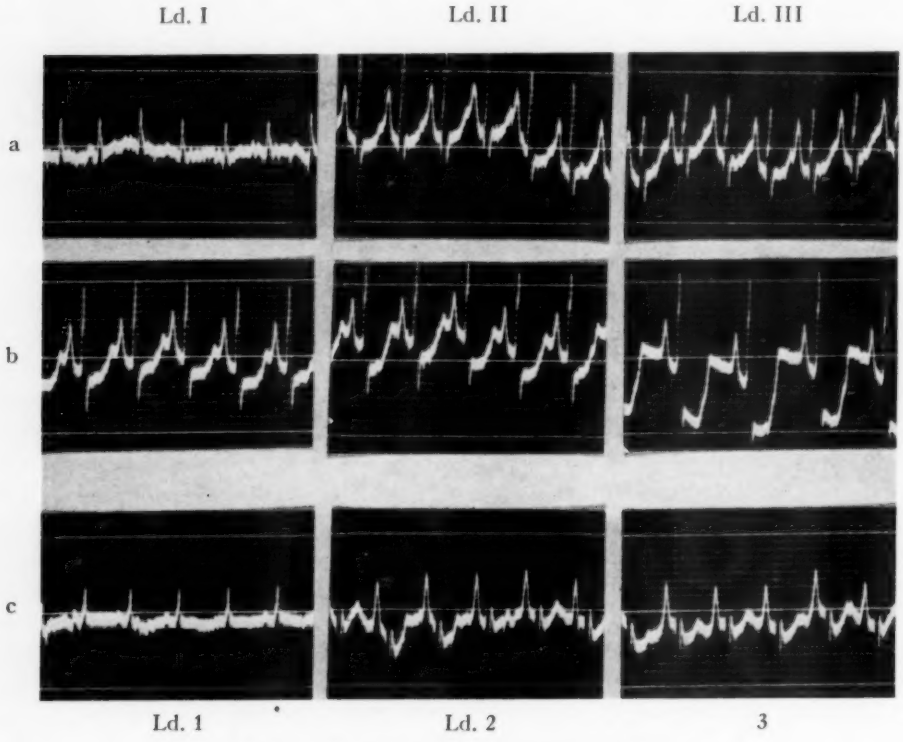

Fig. 3. Experimental pulmonary embolism.

(*a*) Tracing obtained after animal anesthetized.
(*b*) Electrocardiogram after pulmonary embolization. Serial Lead II recordings. The animal died 4 minutes after blood clot was injected into jugular vein. Note that ST_2 takes off progressively further below baseline.
(*c*) Electrocardiogram recorded following pulmonary embolization in another experiment. There has been no significant change in Lead I. The ST segments have become depressed in Leads II and III. This animal was allowed to recover, but died during the night. The lungs were found to be edematous, and the right ventricle was dilated.

the main artery was constricted to less than half its diameter. In each experiment, with one exception, the ST segments were promptly and quite markedly depressed. In one experiment but little change occurred. Such depression of ST occurred in all leads in two experiments and in Leads II and III in three experiments. In two of these latter three experiments, ST_1 eventually became depressed as the obstruction was continued. When the ligature about the artery was released, the ST segments returned to the base line and again promptly became depressed with retightening of

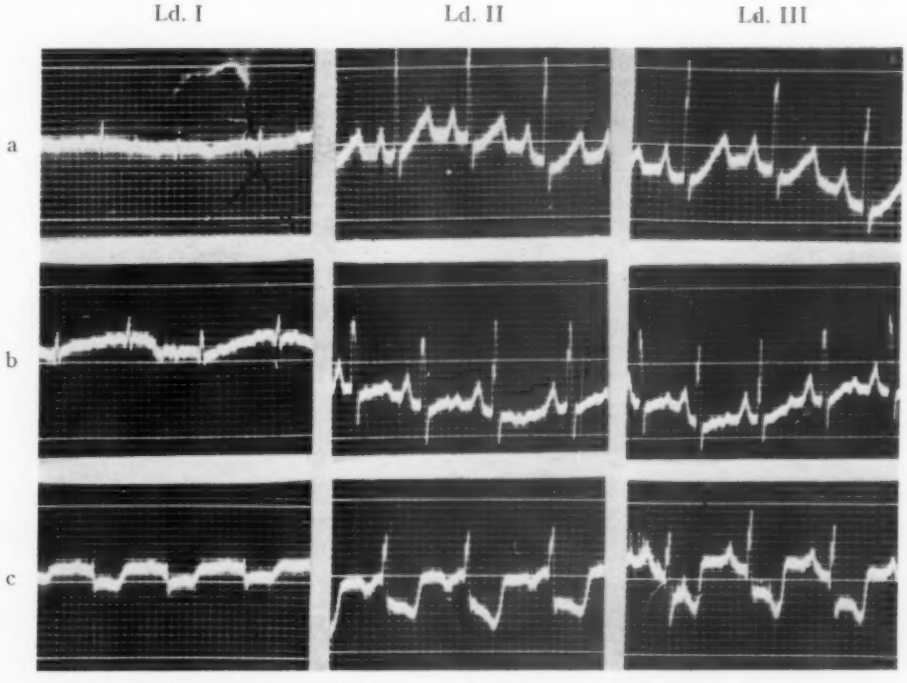

FIG. 4. Pulmonary artery ligation, sympathetic and vagal section experiments.
(*a*) Electrocardiogram obtained following anesthetization of animal.
(*b*) Animal sympathectomized. T-waves become notched and of lower voltage. There is no change in the ST segments.
(*c*) Pulmonic artery obstructed by partially tightened ligature. Note marked depression of ST segments in all leads. T-waves become inverted.

(*Continued in figure 5*)

the ligature. The T-waves were reversed in direction in Leads II and III, or in Lead III alone, in 7 of the 11 observations made upon these five dogs.

Thus electrocardiographic changes similar to those noted in dogs following embolization of the pulmonary arterial tree were produced by mechanically obstructing the artery before its bifurcation. Therefore, it would seem demonstrated that stimuli arising from the immediate lodgment of emboli within the lung vascular bed do not reflexly cause the electrocardiographic findings noted. It seems likely that the degree of mechanical obstruction is the important factor. Visible and marked right ventricular

dilatation always accompanied, and, as far as could be determined, preceded such changes in the electrocardiogram.

V. Vagal and Sympathetic Section and Pulmonary Embolization or Obstruction to the Pulmonary Artery (Figures 4, 5)

In one embolization experiment, section of the vagal-sympathetic cord in the neck did not alter the electrocardiographic findings. In the artery ligation experiments, the vagi were separated from the vagal-sympathetic cords and cut once; thoracic sympathetic ramisection and ganglionectomy plus severance of the sympathetic cords in the neck was performed once; section of the cervical sympathetic cords was done once. The animals undergoing preliminary sympathetic section or ganglionectomy were later subjected to vagal section and the experiment was then repeated. The vagal-sympathetic cords in the neck were sectioned once. In none of these experiments was there noted any alteration in the type of electrocardiogram obtained following ligation of the pulmonic conus. Therefore, it seems

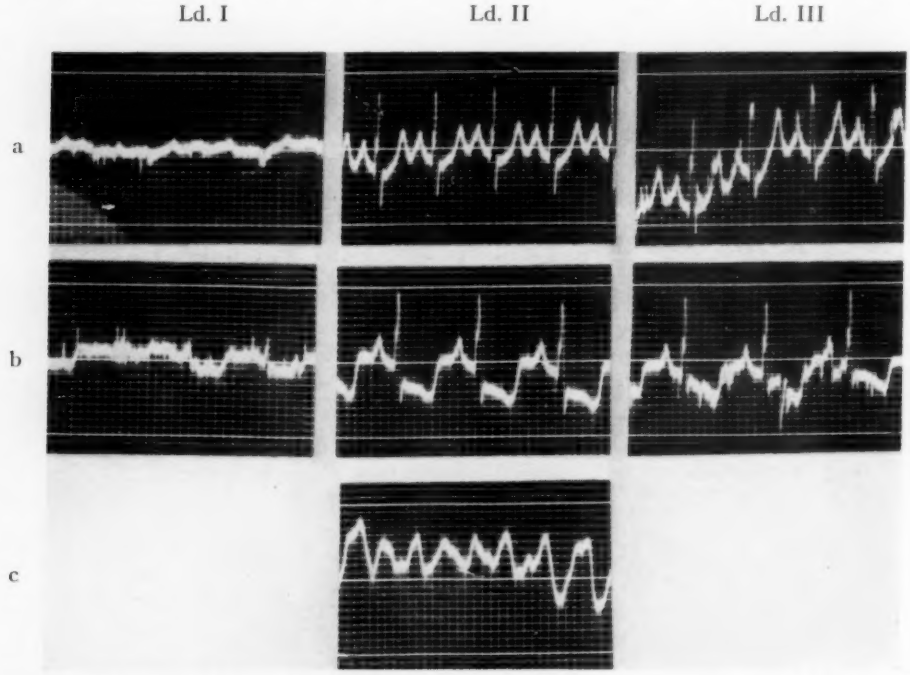

Fig. 5. Pulmonary artery ligation, sympathetic and vagal section experiments (continued).
(*a*) After tracing 4*c* was obtained the ligature about the artery was loosened. The dilatation of the right ventricle markedly diminished. Both vagi were then cut in the neck and this electrocardiogram was then recorded. The T-waves are larger than in 4*b*.
(*b*) The ligature about the conus was partially tightened again. The electrocardiogram then recorded is similar to that shown in 4*c*. There is marked ST segment depression and T-wave inversion.
(*c*) Ventricular fibrillation occurred a few minutes later.
Identical curves to those recorded above were obtained in a similar experiment when the vagi were cut first.

unlikely that reflexes mediated through the vagi or sympathetics play any rôle in producing the electrocardiograms described above.

VI. Comparison of the Electrocardiograms Recorded after Experimental Pulmonary Embolization, Ligation of the Pulmonary Artery, Asphyxia, Hemorrhage (Shock) and Hemorrhage Plus Coronary Artery Constriction

The consistent finding in the electrocardiogram obtained following artificial pulmonary embolization or partial ligation of the pulmonary artery is depression of the ST segments. Asphyxia, in one animal, produced a

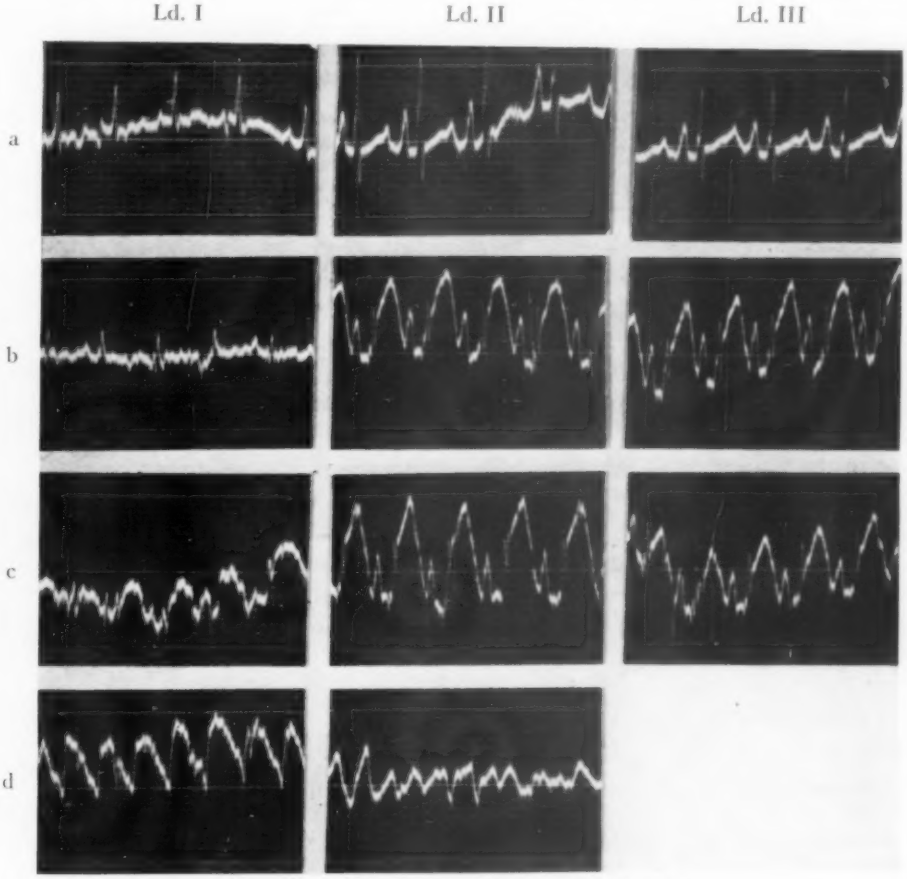

Fig. 6. Coronary artery ligation experiment.

(*a*) Electrocardiogram after induction of ether anesthesia and exposure of the heart.
(*b*) After ligature of posterior coronary arteries. There is little change in Lead I. The ST segments take off high in Leads II and III.
(*c*) Anterior coronary arteries ligated. Leads II and III remain much the same as in experiment *b*. However, ST, now has a high take off also.
(*d*) Terminal arrhythmia—ventricular tachycardia in Lead I, changing to ventricular fibrillation in Lead II.

These tracings do not resemble those obtained after obstruction of the pulmonary arterial system.

graph similar to that of coronary thrombosis with elevation of the ST portion of the curve. Hemorrhage and shock produced no changes in the ST segments and T-waves. Hemorrhage plus coronary constriction were followed by graphs more or less similar to those noted after coronary occlusion. Coronary occlusion causes elevation of the ST segments in one or more leads. Therefore, it seems unlikely that anoxemia due to insufficient coronary flow plays any important rôle in the electrocardiographic changes noted after pulmonary embolization.

Summary and Conclusions

From the experiments cited above we conclude that the changes in the electrocardiogram observed after pulmonary embolization or infarction are due to dilatation of the right ventricle. These changes are depression of the ST segments in one or more leads, most frequently in Lead II, and often reversal of the direction of the T-waves in Lead III and the precordial lead. The evidence adduced indicates that myocardial anoxemia or reflexes mediated through the vagi or sympathetics play no rôle in the production of the above electrocardiographic abnormalities. However, it is obvious that any major occlusion of the pulmonary circulation must lead to a very considerable diminution in the output of the left ventricle and this factor probably plays an important rôle in the occurrence of death, and, further, may play some rôle in the arrhythmias which develop. Similar electrocardiographic aberrations occur both in clinical and experimental lung embolism, and in experimental narrowing of the pulmonary artery. In both clinical cases and in the experiments reported here, arrhythmias are not uncommon. No electrocardiographic changes of note, other than terminal arrhythmias, followed severe hemorrhage in the experiments performed by us.

It seems probable that shock or rapidly produced severe anemia may induce curves similar to those of coronary occlusion if the coronaries are already narrowed. However, these curves are not similar to those obtained after pulmonary embolization.

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SUBACUTE BACTERIAL ENDOCARDITIS FOLLOWING THE REMOVAL OF TEETH OR TONSILS *

By L. Feldman, M.D., and I. M. Trace, M.D., F.A.C.P., *Chicago, Illinois*

It has been the opinion of many investigators that the upper respiratory passages and the mouth harbor foci which act as the most common portals of entry in subacute bacterial endocarditis. There is a good deal of bacteriologic and immunologic work which tends to support this opinion, besides suggesting the important conclusion that transient bacteremia is not an infrequent occurrence in the seemingly benign infections in this region. The literature is too voluminous to be given in detail.

Horder,[1] more than 25 years ago, referred to the "undoubted fact" that the infective agent in most of the cases of subacute bacterial endocarditis was derived from the mouth. Libman [2] stated that the non-hemolytic streptococcus (viridans) causing the disease may be found in tooth sockets, roots of teeth, infected gums, accessory sinuses, and in all parts of the throat. He also expressed the belief that these cocci are entering the blood stream all the time, even when these foci are quiescent. White [3] believes that the non-hemolytic streptococcus is an occasional invader of the blood stream. Thayer [4] observed that many cases of subacute bacterial endocarditis originated from pyorrhea alveolaris or abscesses about the roots of the teeth. Swift [5] pointed out that the non-hemolytic streptococcus is a normal inhabitant of the mouth and is frequently found in pure culture in apical dental abscesses. Blumer [6] observed a case in which it was possible to isolate the streptococcus from a root abscess at the time that it was present in the blood.

Okell and Elliott [7] pointed out that focal infection about the teeth, gums, pharynx and accessory sinuses plays a great part in the development of subacute bacterial endocarditis. They showed that in patients with severely septic mouths, non-hemolytic streptococci may enter the blood stream in the absence of any obvious trauma. A single examination of the blood of 110 patients with septic mouths revealed that in 10 per cent the cocci were present in the blood. They conclude that this "leak," which may be of little consequence in the normal person, might determine the infection of diseased or malformed valves.

Oille, Graham, and Detweiler,[8] in a discussion of streptococcus bacteremia in endocarditis, pointed out that, in their opinion, endocarditis more frequently follows tonsillitis in children than is commonly believed. Libman [9] stated that the onset of subacute bacterial endocarditis can occur with the onset of acute tonsillitis. He [10] also stated that invasion from an acute focal infection may be the cause for recurrences in recovered cases. Re-

* Received for publication December 17, 1936.
From the Department of Medicine, Mount Sinai Hospital, Chicago, Illinois.

cently, Weiss [11] showed that the onset of subacute bacterial endocarditis is frequently immediately preceded by an acute infection of the upper respiratory tract, tonsillitis, or grippe.

Kreidler,[12] in a study of the organisms isolated from 14 cases of subacute bacterial endocarditis, showed the serologic individuality of each of the non-hemolytic organisms. Cross agglutination or complement fixation was not demonstrable. Immune bodies were present in the patient's serum against the homologous invader only. The same immunologic and bacteriologic heterogenicity exists among the streptococci of the upper respiratory passages, which is probably the only location in the body in which such a flora is constantly present and which can furnish the necessary nidus and portal of entry for the establishment of an endocardial implantation.[11] Hooker and Anderson [13] studied the colony strains of streptococci from 100 specimens of sputum and found the dominant aerobic strain to be the non-hemolytic type. This parallels the observation of blood cultures in subacute bacterial endocarditis. They also showed the same heterogenicity among their non-hemolytic streptococci as Kreidler noted in his blood cultures. Arnold's [14] series of throat cultures showed 91 per cent of the non-hemolytic streptococcus before an epidemic of influenza and 100 per cent during it.

A good deal of investigation has been carried out on the bacteriology of extirpated tonsils. Kilduffe and Hershon [15] found non-hemolytic streptococci in only 5 per cent in a series of 409 tonsils, while Polvogt and Crowe [16] found them in 91 per cent of their 100 cultures from removed tonsils. Bartlett and Pratt [17] found the non-hemolytic streptococci in 25 per cent of their cultures.

Henrici and Hartzel [18] examined 46 dental pulps and found the non-hemolytic streptococcus in 28. They concluded that in approximately 50 per cent of the vital teeth, invaded by caries or surrounded by pyorrhea, the pulp is already infected by this type of streptococcus. Lucas [19] made 364 cultures from pulpless teeth and found the non-hemolytic streptococcus in 275 of them. Cultures were also made from 120 sockets of pulpless teeth. Those that were not curetted or sterilized were positive for this streptococcus in 98, but this organism was found in only six when curetted and sterilized.

Less common portals of entry in subacute bacterial endocarditis are the otitic infections, infections of the genito-urinary tract, as following abortion or instrumentation,[11, 20] phlegmons and wounds,[20] and, lastly, the gastro-intestinal tract.[1]

Libman and his co-workers [21] drew attention to the fact that, with few exceptions, the development of subacute bacterial endocarditis requires the fertile soil of an earlier endocarditis—rheumatic, arteriosclerotic, syphilitic or congenital lesions. It is of interest, in this respect, to cite the case of Hamman and Rienhoff [22] in whom a non-hemolytic streptococcus bacteremia was cured by the excision of an arteriovenous aneurysm, the edges of which harbored the vegetation that fed the blood stream. When the non-hemo-

lytic streptococcus affects sound valves, the infection is of short duration and resembles more the acute type of bacterial endocarditis.[21]

The surgical removal of foci of infection from patients with valvular or congenital heart disease, as a preventive measure, has been advocated for many years, and as a consequence, has been extensively practiced. But that minor surgical procedures, such as extraction of teeth or removal of tonsils, may become exciting causes of subacute bacterial endocarditis is not widely known. It is only in the last several years that such reports have begun to appear, and they are comparatively few. This may be due to the fact that a history of removal of teeth is not sought, that the patient does not deem it important enough to volunteer such information, and that the onset of the disease is insidious. The prevalence of dental sepsis and dental extraction leads one to believe that such a history could be obtained more frequently in cases of subacute bacterial endocarditis. The scarcity of reports following tonsillectomy may be accounted for by the fact that the great majority of tonsil operations are done on children, and usually at an age when the incidence of subacute bacterial endocarditis is conspicuously low.

Tileston [23] reported two cases in which the infection started soon after the extraction of teeth. Rushton,[24] out of 40 patients with subacute bacterial endocarditis, found four that had developed the disease following the extraction of teeth. One had a molar extracted; another, four teeth removed; the third had a number of teeth removed; and the fourth had a few roots pulled. Abrahamson [25] reported two cases that followed the extraction of one or more teeth, and one case following tonsillectomy. Brown's [26] case was immediately antedated by extraction of only one pyorrheic tooth. Vanderhoof and Davis [27] had two cases, one following the extraction of two badly abscessed teeth, the other, following the removal of one tooth. Von Phul [28] reported three cases. In one, all of the upper teeth were removed; in another, one impacted tooth was removed; in the third, two wisdom teeth were pulled. Bernstein's [29] case had two teeth pulled. Weiss [11] studied 364 cases of subacute bacterial endocarditis and found three cases in which the disease followed tonsillectomy; five cases were antedated by the extraction of one tooth each; and two cases followed the removal of more than one tooth each.

On the other hand, that not all of the cases reported as subacute bacterial endocarditis due to operative intervention may safely be attributed to that cause is very well exemplified by the following case, seen by one of us (I. M. T.):

A man, 60 years old, married, painter, had hypertrophic arthritis of moderate severity. His cardiovascular system presented evidence of arteriosclerosis. His teeth and gums were fearfully pyorrheic. He was advised to have his teeth removed as a general hygienic measure. This advice was not followed. Three weeks later he entered the hospital with a low grade temperature, colicky abdominal pains, and blood in the stools. No diagnosis was made. Five days later a cerebral accident occurred, with speech disturbance and hemiparesis. Soon the blood culture became

positive, many petechiae appeared, the spleen became palpable, and infarctions took place. He died eight months later.

Had his teeth been removed, we would have ascribed the endocarditis in this case to the operative procedure. Is it not conceivable that the infection may already be present in some cases when foci of infection are removed? Libman, in a personal communication, states: "At times such intervention is carried out because the patient is not feeling well, it not being known that an endocarditis is already present."

In view of the fact that the non-hemolytic streptococcus is commonly present in and about these foci of infection, operative trauma would appear to offer an opportunity for dissemination of such organisms from the focus by lymphatic or venous channels. The efficient mechanism which exists for cleansing the blood stream of organisms of low virulence that may "leak" in from a focus, fails when the "leak" becomes a "flood." Thus an implantation on diseased or malformed valves is greatly facilitated.

That surgical intervention for the removal of foci of infection is frequently accompanied by a transient bacteremia has been demonstrated many times. Libman and Celler [30] described cases of postoperative bacteremia following trauma. Dobney [31] reported a case that developed a streptococcic bacteremia two weeks following a tonsillectomy. He assumed that a local infected thrombus in the tonsillar fossa fed into the blood stream. Harter [32] pointed out that a positive blood culture may be found following mastoidectomy. Fischer and Gottdenker [33] detected bacteria (staphylococci, streptococci, or pneumococci) in the blood stream of 16 out of 50 patients two hours following tonsillectomy. Okell and Elliott [7] examined the blood for bacteria in 138 patients undergoing extraction of teeth. Seventy-five per cent showed a transient non-hemolytic streptococcus bacteremia within a few minutes after extraction, lasting only several minutes. Even when there was no obvious gum infection, extraction of teeth was followed by streptococcus bacteremia in 34 per cent. The organism isolated from the blood in the majority of the cases was a streptococcus of the viridans type, culturally and serologically similar to the streptococcus derived from the mouth. In general, they found that the degree of the bacteremia depended upon the severity of the infection and the amount of surgical trauma done.

Schottmueller [34] reported a case of bacteremia after a curettage, and Seifert [35] found bacteria in the blood in 22 per cent of his appendectomy cases. Libman [21] regards the non-hemolytic streptococcus as an ubiquitous organism and also as the most important secondary invader with which we have to deal. Hence he cautions that this coccus may be found in the blood of patients suffering from conditions other than endocarditis. This is an important fact to bear in mind.

During the past few years we have been impressed by the fact that a non-hemolytic streptococcus bacteremia with endocardial implantation may occur immediately following a relatively simple operation in an infected

area, about the dental structures or the throat. This led us to determine how many cases of subacute bacterial endocarditis, that were seen in the Mount Sinai Hospital in the last 12 years, dated the onset of their symptoms from some form of surgical procedure, particularly in the mouth or throat.

Out of 38 cases, five definitely gave such a history. These cases are reported here. In a number of others the history was too indefinite to warrant consideration. The relevant facts in the cases in which a history of surgical trauma antedated immediately, or shortly before, the onset of the disease are indicated as follows.

Case Reports

Case 1. A woman, aged 36, married, housewife, was admitted to the hospital August 3, 1935, complaining of fever, weakness, palpitation and dyspnea of six months' duration. At the age of 10 she had a prolonged bout of rheumatic fever. Several years later rheumatic heart disease was discovered during a routine physical examination. She had no symptoms, married at the age of 24, and had one child. In recent years she developed, however, slight dyspnea upon exertion.

About six months before entrance she was advised by her physician to have all of her teeth extracted, because they were infected. Immediately following the extraction, she began experiencing fever and palpitation. Weakness gradually set in, the dyspnea became worse, and she was compelled to take to her bed.

Physical examination revealed a pale, weak, dyspneic and toothless woman. The pulse was 120, regular, temperature 101° F., and blood pressure, 110 mm. of Hg systolic and 65 diastolic. There were a few petechiae in the conjunctivae. The heart was enlarged, conforming to the mitral type. A presystolic thrill was present at the apex. A presystolic and fairly long systolic murmur were heard at the apex. The pulmonary second sound was accentuated. The spleen was enlarged. Blood culture revealed the non-hemolytic streptococcus. She became progressively weaker and died one week after entrance. Autopsy revealed subacute bacterial endocarditis of the mitral valve which was markedly stenosed.

Case 2. A woman, aged 22, single, clerk, was admitted April 4, 1927, because of weakness, chills, and rise in temperature. Ten years previously she had rheumatic fever, and she knew that it gave her a "weak heart." The onset of her complaints dated back 10 weeks. At that time she had a slightly abscessed tooth extracted, and on the following day she developed a chill, followed by fever. The fever persisted and weakness soon followed.

Physical examination revealed a young woman with the typical *café-au-lait* color. The pulse was 114, regular, the temperature 102° F., and the blood pressure, 100 mm. of Hg systolic and 60 diastolic. The heart was only slightly enlarged, but of the mitral type. A long, soft, blowing systolic murmur was heard at the apex. The pulmonic second was accentuated. The spleen was palpable. Blood culture was positive for the non-hemolytic streptococcus.

She became progressively worse, developing petechiae, and then multiple embolizations. She died eight months following admission. Autopsy was not permitted.

Case 3. A man, aged 40, married, merchant, was admitted November 16, 1927. He complained of chills and rise in temperature of six weeks' duration.

He was perfectly well until six weeks before entrance, when a tonsillectomy was done. Two weeks later he developed a chill with a rise in temperature. He had only two fever-free days in the last six weeks. He had rheumatic fever at the age of 15, since which time he had known that his heart was affected, but it gave him no discomfort.

Physical examination revealed a well developed man, who was quite pale. The temperature was 103° F., pulse 124, and blood pressure, 130 mm. Hg systolic and 80 diastolic. The heart was not enlarged, but a soft systolic murmur was heard at the apex. Petechiae were present in both conjunctivae. The blood culture was positive for the non-hemolytic streptococcus.

He became progressively weaker. The spleen became palpable, and evidence of embolization soon began to appear. He died three months later. Autopsy was not permitted.

It is possible that a local infected thrombus in the tonsillar fossa fed the bacteria into the blood stream; hence the reason for the delayed onset.

Case 4. A woman, aged 24, single, stenographer, was in perfectly good health, although she knew that she had "heart trouble" since childhood.

About 10 days following the extraction of one abscessed tooth, she began experiencing loss of strength, chills, and anorexia. After two weeks of self-medication at home, she decided to enter the hospital.

Examination revealed a pale young woman; the temperature was 100.5° F., the pulse 100 and regular, and the blood pressure, 110 mm. of Hg systolic and 70 diastolic. The heart revealed typical findings of rheumatic heart disease of the mitral valves. The spleen was palpable, and the blood culture was positive for the non-hemolytic streptococcus a week after entrance.

Splenic and renal infarcts became evident a few weeks later, and the liver became palpable. She lingered on for eight months, having acquired the typical *café-au-lait* color, and moderate clubbing of the fingers, before death.

Case 5. A physician, aged 48, married, was in good health, except for some joint pains of a few years' duration. He never had rheumatic fever, or any other acute infection, nor did he have any symptoms referable to the cardiovascular system.

Examination revealed marked pyorrheic teeth, and a mild degree of rheumatoid arthritis. The roentgen-ray, however, did not show any changes. Temperature, pulse, and blood pressure were not abnormal. The blood count, too, was within normal limits. Because of his arthritis, his teeth were extracted. A thorough job was done, in a rather "wholesale" manner.

Several weeks later, August 4, 1929, he was admitted to the hospital because of severe pains in his calf muscles. He also complained of some weakness and lack of energy. Examination at this time revealed tender areas, the size of a silver dollar, scattered throughout the calf muscles. The liver was palpable, but not the spleen. The heart findings remained normal.

Soon he began to have a low grade fever, and his pulse rate became elevated. Anemia became manifest. Evidence of infarction of the spleen and kidney appeared, and soon after the spleen became palpable. The blood culture, however, remained negative.

Seven months after the onset, a diastolic murmur, heard best in the third left interspace, appeared, and became more intense and prolonged as time went on. At about the same time the tips of his fingers became pink, as if dipped in a coloring solution. Towards the end of the disease, which lasted 14 months, his blood became positive for the *Streptococcus viridans*. He finally died of an attack of pulmonary edema.

In this case, it is highly probable that a preëxisting arteriosclerotic process facilitated valvular implantation. A bicuspid aortic valve was another possibility.

Many interesting and important problems arise from consideration of these cases. If proof were needed that infection in subacute bacterial endocarditis may be derived from teeth or tonsils, such cases would supply the

necessary evidence. Paradoxically, then, they emphasize the importance of removal of septic foci, but they stress the need for great caution.

How should caution be employed? How may this desirable prophylactic procedure be prevented from becoming an exciting cause? It is evidently not the number of teeth extracted, for the infection has followed the removal of only one tooth almost as frequently as following several. Should only definitely abscessed teeth be removed, and teeth that are firmly fixed and require much manipulation [25] be left in place? Yet, pyorrheic and loose teeth have many more organisms in their pockets, and their removal, no matter how easily accomplished, would still not be devoid of danger. Brown [26] thinks that local anesthesia by infiltration may be instrumental in carrying organisms into the blood from the infected field. However, the pressure of the injected fluid and the epinephrine that it usually contains may produce the opposite effect by compressing and constricting the lymphatic and vascular channels. Preliminary vaccination with an autogenous vaccine from the gums and throat seems a rational procedure, but it is not feasible in the greatest number of cases.

It seems to us that the problem of prevention of post-operative nonhemolytic streptococcus bacteremia, which may become a tragedy in people with valvular or congenital heart disease, revolves itself largely around two points.

First and foremost is the condition of the patient at the time of these, apparently minor, surgical procedures. The natural bactericidal powers come into play as soon as bacteria invade the blood stream. If it were not for them, many more cases of serious complications following the removal of septic foci would be seen. It is logical, then, to assume that patients who are anemic and in a " run-down " condition have the least amount of resistance. Since the removal of foci of infection is mostly an operation of " election," the physician should proceed to " build up " the general condition of the patient first and send him to the dentist afterwards.

The intelligent dentist, we are sure, welcomes such an arrangement, and is glad to have the physician share the responsibility. But the more usual practice today is that the dentist, seeing the patient first and not being aware of the lurking danger, proceeds with the extraction. It is only when complications arise that he seeks the advice of the physician.

Libman [36] states: " I am in favor of getting rid of all foci of infection in patients with valvular or congenital heart disease. But one must be cautious as to when to carry out the procedure, and as to how much is done at a given time. My procedure is to improve the patient's general condition whenever possible, before any operative work is carried out."

The second point, in our opinion, is the dental surgical technic. The procedures employed before and immediately after the operation are just as important as the operation itself. Before any surgical procedure in the mouth is undertaken, a thorough scraping and cleaning of the teeth should be done, thus removing myriads of bacteria that would otherwise contami-

nate the operative field. About a week later extraction may be begun, removing one or two teeth at weekly intervals. Immediately following the extraction, the socket should be curetted, and treated with antiseptics. Rosenow [37] advises the use of 95 per cent carbolic followed immediately by alcohol. It has been shown above [19] that cultures from such sockets are rarely positive. Packing is advocated by some dental surgeons to prevent the accumulation of clotted blood, which might form a nidus for bacterial growth. There is no agreement on this point.

Conclusions

1. *Septic foci* in the mouth and upper respiratory passages are regarded as undoubted portals of entry in subacute bacterial endocarditis. Therefore, as a prophylactic measure in people with valvular or congenital heart disease, these foci should be removed.

2. From time to time, however, cases of subacute bacterial endocarditis are seen that are caused by the extraction of septic teeth or the removal of infected tonsils. Five such cases are reported.

3. In view of the fact that the non-hemolytic streptococcus is commonly present in and about such foci of infection, operative trauma appears to offer an opportunity for a transient bacteremia. When this does occur, the diseased or malformed valves become the required fertile soil, and implantation is facilitated.

4. To prevent such catastrophies, the following measures are proposed:

Patients who do not appear in good health should be first "built up," according to the methods outlined, before any operative work in the mouth or throat is undertaken.

In all cases of contemplated extraction of teeth, especially in young patients, inquiry should be made by the dental surgeon as to whether the patient has ever been examined for heart trouble and any lesion found.

Finally, strict adherence to the dental surgical technic discussed is urged, when extracting teeth in patients who have an acquired or congenital heart disease.

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MYOCARDOSIS: A PLEA FOR EARLY RECOGNITION OF CORONARY ARTERY DISEASE *

By Aaron E. Parsonnet, M.D., C.M., F.A.C.P., *Newark, New Jersey*

In 1926, Riesman [1] proposed the term "myocardosis" as a logical substitute for the meaningless and outworn concept of "chronic myocarditis." Again, in a paper read before the American College of Physicians in 1929,[2] he pointed out the inadequacy of "chronic myocarditis," especially when used in describing the cardiac diseases of middle life.

The favorable reception accorded our first essays on "myocardosis," [3, 4, 5] and the general interest aroused by the introduction of this newer concept of heart disease, as seen in the middle and advancing age periods, prompted the authors to a further and deeper consideration of the problem and a volume devoted entirely to this subject was the result.[6] Since 1932, however, although this term is finding wider use,[7-16] much clarification and correction of misconceptions has become absolutely necessary. It is the object of the present paper to crystallize and bring into greater relief the cardinal points in diagnosis, both clinical and electrocardiographic. Four typical cases have been carefully selected from a large mass of clinical material. Histories with electrocardiographic findings are presented in detail. Note that two of these are of young people, whose ages precede by quite a few years the traditionally accepted "middle age period." Each of these histories stresses a particular phase in the transition from myocardosis to definite coronary disease, at the same time bringing out the other features of the myocardosis syndrome. To become proficient at all in early recognition of the disease, all symptoms and complaints, no matter how trivial and relatively unimportant these may seem on the surface, must be carefully considered and properly evaluated.

In view of the steady advances of cardiology it is time that the terminology of earlier days yield to newer concepts. It seems unnecessary to cling to a term like chronic myocarditis which is both incorrect and inadequate, particularly when applied to the early phases of coronary artery disease.[17, 18]

From a histo-pathologic point of view, myocardosis is associated with and apparently is dependent upon the *gradual* nutritional atrophy of the parenchymatous elements of the heart. Even slight alterations in the metabolic balance of the myocardium are sufficient to cause marked subjective as well as objective symptoms. Our chief concern is with the recognition of the earliest phases of myocardial change which inevitably precede the recognition of the more serious coronary artery disturbances.

The keener clinicians of an older day were fully cognizant of the fact that there existed non-inflammatory cardiac lesions which were clinically

* Received for publication February 16, 1937.

significant. Quoting from a letter written by Thomas Percival in 1784 [19] concerning one of his cases:

> A gentleman aged upwards of fifty, who had been, for several years, subject to frequent attacks of a most alarming and oppressive sensation in his breast, which he knew not how to describe. This symptom was attended with a pain about the middle of the sternum, inclining to the left side; and he was generally affected, at the same time, with a pain in his left arm where the deltoid muscle is inserted. I apprehended his disorder to be what Dr. Heberden hath so accurately described under the name of Angina Pectoris. Nothing afforded such instantaneous relief as venesection or vomiting. He died; and his body was examined by Mr. Allen, an ingenious surgeon, who favoured me with following account of the dissection: The heart and aorta descendens were in a sound state; very little water was found in the pericardium, or mediastinum.

Percival wrote to Heberden about this case and the reply again demonstrates the marvelous clinical sense of the master clinician: [19]

> The dissection of this sufferer by the angina pectoris, as well as that of a few others, which I have heard of, teaches us, that the disease is neither owing to inflammation, nor to any malformation of the parts. We must not therefore seek the cure amongst the means which lower the *vis vitae;* and we need not despair of finding it elsewhere. But we should not expect to find it very soon, when we consider how little success has attended all our searches after a remedy for the gout, and for some other distempers, with whose natures we have had, for some thousand years, such abundant means for being acquainted.

It is apparent that Dr. Heberden felt the need for a reason to explain and atone for the lack of concrete pathology in this group of cases, but nevertheless made a clear distinction between the inflammatory and non-inflammatory underlying causes. Again, in his "Commentaries on the History and Cure of Disease," [20] Heberden makes it a point to differentiate certain ill-defined chest pains from "angina pectoris." (The former were unfortunately obscured later on by the term "pseudo-angina," a meaningless phrase which is still very hard to eradicate from our medical literature.) In contrast to his classical description of angina pectoris, he has this to say of them:

> Besides the asthma, hysteric oppressions, the acute darting pains in pleurisies, and the chronical ones in consumption, the breast is often the seat of pains, which are distressing, sometimes even from their vehemence, oftener from their duration, as they have continued to tease the patient for six, for eight, for nine, and for fourteen years. There have been several examples of their returning periodically every night or alternately with a headache. They have been called gouty and rheumatic, and spasmodic. There has appeared no reason to judge that they proceed from any cause of much importance to health (being attended with no fever), or that they lead to any dangerous consequences; and if the patient were not uneasy with what he feels, he needs never to be so on account of anything which he has to fear.

This description with but few modifications could readily fit into the myocardosis syndrome; and so, to the careful observer of even a hundred years ago, a symptom-complex presented itself which differed from angina

pectoris as well as from acute or chronic cardiac failure. To the lasting credit of Heberden, this distinction was made without the aid of instruments of precision and the diagnostic refinements of our present day.

Hamburger,[21] in a recent (1935) paper entitled, "Angina Pectoris without Coronary or Aortic Disease," cites a group of cases, most of which could be much more accurately classified under myocardosis. All or most of these have the vague symptoms and lack of positive findings seen in the myocardosis syndrome. Many names, which do anything but enlighten, are bestowed upon myocardoses: "tobacco angina," "angina pectoris vasomotoria," "angina of anemia," "secondary angina," though euphonious and high-sounding, have small basis in fact and only serve to cloud the issue at hand rather than clarify it. Only by uniting this heterogenous group of conditions and accepting them all as manifestations of myocardosis, may we ever hope to treat them early enough to cut down the steadily mounting numbers of deaths due to coronary artery disease.

Kaufmann,[22] in his attempt to find the earliest possible manifestations of coronary artery disease, carefully reviewed a large series of cases in which a diagnosis of advanced coronary disease had been made; he found that three symptoms led all others in their frequency of occurrence. Not only were these the first to appear, but they could also be traced back for many years when carefully searched for. These symptoms, dyspnea, palpitation and substernal distress were aptly designated the "three steps to heart failure." Since we, too, are hunting for the earliest diagnostic criteria, it might be well to reëxamine Kaufmann's steps to cardiac failure, for in spite of our instruments of precision in early diagnosis the history is of prime importance. To take a hurried and superficial history, quickly scan negative electrocardiograms and roentgen-ray reports, and finally send the patient back to his strenuous life with assurances that all is well, will inevitably bring disaster to the patient and embarrassment to the doctor. A careful history is essential in these cases and the following are the most important features for which to hunt.

Symptomatology. Dyspnea after effort, though a difficult symptom to evaluate properly, is of great importance from a diagnostic standpoint. Of course, the questioner must overcome the patient's natural distaste for admitting physical decline of any type; he must also cope with unconscious exaggeration of all symptoms by a different type of individual. A method of eliciting an accurate estimate of whether dyspnea is really present is to find out whether the patient is more dyspneic at present, after an accustomed bit of work, walking or stair-climbing, than a year or so ago. Most patients will be able to answer such questions with greater accuracy and the questioner will have a reply applicable to the patient rather than one that has to be fitted into a group average. In general, breathlessness is to be regarded as one of the important features of myocardosis. In its early phases it may assume atypical forms. This symptom may often be obscured by the co-

existence of two or more conditions, and such possibilities must be always borne in mind by the examiner.

Next in importance as a symptom of early myocardosis is *palpitation.* Such heart consciousness varies from a mere awareness of the heart's activity to a painful pounding in the precordium. Numerous word designations are given to this symptom, the most characteristic being thumping, skipping, knocking, fluttering, shivering. Although in the younger age groups this symptom is not indicative of any special cardiac pathology, in the middle age period, on the other hand, a vast majority of those presenting such a symptom have associated myocardial or vascular changes. The clinician must consider that palpitation may also be caused by things extracardiac such as emotional disturbances, gastrointestinal upsets, other lesions in the chest and mediastinum, liver and gall-bladder disease, and thyroid dysfunction. These must be properly eliminated before the symptom can be considered cardiac. In the middle age group, more than a quarter of those complaining of palpitation have no evidence of cardiac arrhythmia and this is the very group that must be most carefully considered in diagnosis. The appearance of palpitation after habitual or customary effort should be regarded as an especially significant symptom of myocardosis, even in individuals who present no other evidences of cardiac involvement. When occurring in vigorous, middle-aged individuals, it cannot be lightly dismissed as it forms either alone or in conjunction with dyspnea and substernal distress one of the milestones in the progress of degenerative changes developing in the cardiovascular system.

Substernal distress is probably the symptom most easily recognized by the doctor and patient. This symptom also has a whole gamut of descriptions ranging from a mere heaving of the chest to the vise-like constriction of angina pectoris. In the myocardotic, the symptom is commonly described as a feeling of compression or tightness usually localized in the sternum and not the precordium. Often no reference is made to the heart at all by patients presenting this symptom. In myocardosis there is almost none of the radiation present, which is so frequently experienced later when the full-blown pain of severe coronary artery disease supervenes. This symptom comes on most commonly after muscular effort and very rarely as a result of mental strain or gastrointestinal upsets.

Worthy of consideration are the vague but no less important *gastrointestinal symptoms* of early myocardosis.[23, 24] The patients, as a rule, complain of " nervous indigestion," epigastric fullness, burning sensations in the midepigastrium, nausea and, more rarely, vomiting after meals. It is here that a careful system by system review in obtaining the history is most essential, for only in this way may one be able to discover the three cardinal symptoms already mentioned. Should the questioner focus all his attention upon the gastrointestinal tract alone, he will miss many of these cases. Until the index of suspicion of myocardosis, whenever there are gastric symptoms,

becomes much higher than it now is, we will continue to allow many of our patients to go unrecognized.

Finally, *insomnia without apparent cause, easy fatiguability* and even *personality changes,*[6] will at times be the only clues that will guide the clinician along the cardiac trail for their explanation.

Dyspnea, palpitation, substernal distress, indigestion and insomnia are therefore the symptoms for which to seek in every patient of middle age. Should such an individual suffer from early coronary artery disease, one or all of the symptoms may be discovered without in any way suggesting heart disease to him. For preventive medicine to assume a real meaning, every doctor must familiarize himself thoroughly with this symptomatology of myocardosis.

Objective Findings. Although the history has been stressed repeatedly as the mainstay in a diagnosis of early or advanced myocardosis, there are several objective findings to help. The physical examination in a classical instance is essentially negative; urinalysis, blood count and differential count are within normal limits, and the teleroentgenogram reveals no cardiac enlargement; Bierring [9] feels that, in the electrocardiogram, early left axial rotation with altered T-waves in Lead I is significant of early myocardosis, but in my experience such an electrocardiogram can no longer be considered as indicative merely of myocardosis changes; such alterations in the tracings in my opinion are to be looked upon as signs of severe coronary damage. The electrocardiogram in early myocardosis shows no changes of any appreciable degree. We are left then, as far as objective methods go, with only the methods used in evaluating changes in functional response to help us.

Before attempting to interpret correctly the numerous cardiac function tests, it should be borne in mind that the difference between the normal responses of individuals at various age periods of life becomes greater as the age increases. Thus the tables of standards for various age and sex groups may be more accurately estimated. In the younger age groups the line between the normal and abnormal can be more clearly drawn than in middle and advanced ages; factors not considered significant in the young are of great importance in the latter groups. Overweight, habits, occupation, all make individual estimation more difficult. Two children of the same age should give similar effort response to a single test, two individuals of the same middle age group may vary considerably in their response without either one being considered deficient.

Weiss [25] has shown that a *reduction of vital capacity* is an early sign of circulatory insufficiency. This test is simple and requires very little apparatus. It may be performed in any office on patients suspected of myocardosis. There are several modifications, such as testing before and after measured effort. Within 85 per cent of the established standards of Myers [26] is considered normal, below 80 per cent is significant of lessened myocardial function.

Frost [27] has perfected a *cardio-respiratory test* to represent graphically the measured heart load. This test combines both the use of the sphygmomanometer and the spirometer for the estimation of myocardial activity. It has been employed with some degree of success for the last few years by some of the larger insurance companies. It is doubtful whether it would be practical to adopt this method for average office routine.

Pulse rate tests for the estimation of cardiac function have been in use for many years. An increase of 25 per cent over the resting rate after measured effort is regarded by Kaufmann [22] as normal when applied to the middle age group. Most of these tests consist in the determination of the exact time it takes for the pulse to return to normal after exercise; five minutes is the absolute upper limit for the middle-age group. Any delay beyond this period is evidence of lessened myocardial reserve.

Blood pressure tests may also be employed to advantage. After taking the pressure at rest, the patient is exercised; then the blood pressure is taken once more. If it rises more than 20 mm., and remains elevated for more than 10 minutes, the response may be assumed to be abnormal.

The breath-holding test is of distinct practical value. The patient's pulse rate is determined at rest, he is then instructed to hold his breath as long as possible. Normally, the pulse will drop from 15 to 18 beats per minute; absence of such a drop always points to lessened myocardial reserve. However, it is difficult to say exactly at just what point the degree of variation is sufficient to indicate impairment of myocardial function.

Eyster,[28] in his work on *venous pressure,* found that a pressure of over 300 mm. of water signifies early myocardial failure. Although this observation may eventually be of value in the early recognition of myocardosis, it is still too complicated a test for the average practitioner to perform in his office. Many hospitals are not equipped for its routine performance.

These are the chief tests for the objective recognition of myocardosis. Like all functional tests, their correct interpretation depends in great measure upon sober judgment and clinical acumen.

Treatment. Having considered the essential criteria for the recognition of myocardosis, the question of immediate moment is what can be done for the myocardotic in order to slow the progress of this insidious and progressive disease, and stave off his first coronary seizure. Treatment may be summed up in one word—MODERATION. Moderation in all things will achieve for the myocardotic vastly more than any method of involved therapy or drug medication. With this in mind, mental and physical relaxation is the first step in the treatment. The patient should be persuaded to reduce his business activities so that he will not be forced to go at top speed during working hours. An hour or two in bed every afternoon in order to relax, not necessarily to sleep, will help materially in reducing the cardiac load. A full night's sleep of at least eight hours is absolutely essential; therefore evening parties should be as few as possible. Of equal importance but much harder to achieve is mental relaxation. It is difficult,

indeed, to control a patient who takes his business worries to bed with him, yet the error in doing so must be explained to him gently, diplomatically, but firmly. The greatest care must be taken by the physician when laying down the rules not to make the patient too heart-conscious for this will defeat the entire treatment.

The patient is to be encouraged to take up hobbies which are not too strenuous and in which he is genuinely interested, so that he will become thoroughly absorbed in them and at the same time relaxed. Playing games such as checkers and chess, attending the theater, cinema or concert, are also to be encouraged as a means of mental relaxation. Gambling in any form is to be definitely discouraged because of the mental tension rather than relaxation which it develops. For the same reason, reading of exciting books and attending exciting plays and movies are also inadvisable. Moderate exercise is decidedly beneficial, but tennis and its related games, hockey, handball, soccer and baseball are surely not the games of choice for such patients. Golf seems to be the type of game most suitable, but even here, nine holes would be better than a full eighteen. For the man who does not care for golf, a gymnasium with carefully graded and supervised exercises is excellent. If any exercise is to be taken at all, it must be regular and not in spurts, as sudden strain after a long rest may be very harmful. In other words—moderation. It is also very essential that the patient rest appropriately after effort.

A rarely discussed but very vital problem is the question of sexual exertion and here too moderation is of paramount importance. There are many cases of anginal attacks precipitated by sexual intercourse.

Overweight is another factor that must be brought under control for best results. As a rule, all that is necessary is a carefully balanced diet, and irksome restrictions should be avoided as much as possible. Drugs for reducing, in the absence of endocrine dysfunctions, are of course entirely contraindicated. Reduction of weight is to be a slow and gradual process with a minimum of discomfort to the patient. The man whose weight is satisfactory may be on a full diet with no restrictions except a warning against overeating at any one meal. Alcoholic beverages may be taken in moderation, but any hard drinking is definitely forbidden. The same is true of smoking; if excessive it should be reduced, but not cut out entirely.

Last but not least, the patient's health must be generally improved by eliminating as much as possible all foci of infection. General conditions such as diabetes or lues receive special treatment. A thorough physical examination at least every six months is essential to complete care in these cases.

Prognosis. In the untreated case of myocardosis, the ultimate prognosis depends upon the age of the individual at the time of onset of the condition; the outlook becomes more serious the younger the patient. Individuals seen with myocardosis in their late thirties or early forties often succumb during

their first occlusion. In such cases the postmortem examination may reveal little or no gross pathologic changes. In the myocardotic of 50, the prognosis is still guarded; in this group, however, the symptoms of stenocardia may be present for months or even several years before the fatal attack occurs. Such hearts often show well advanced coronary artery disease with patches of scarring. Myocardosis developing in the next two decades is relatively benign. Here one often finds extensive areas of scarring, areas of infarction and at times aneurysmal dilatations, diffuse scarring and myocardial calcification. Strange as it may seem, such findings are frequently met with in patients who have very few symptoms during life. The most plausible explanation for this apparently paradoxical phenomenon is that the older the heart, the greater has its collateral circulation become. Moreover in the older patients there is much less demand upon the heart than in the younger groups. Therefore, with a decrease in cardiac work, the diminished blood supply can supply the myocardium adequately.

Having reviewed the symptoms and objective findings of early myocardosis, it will help materially to crystallize the entire picture by presenting at this time the clinical course of the cases which were mentioned earlier in this paper. The histories cited here are from my own office files. They serve to give a picture of the condition as it is seen in private practice, and illustrate the decided tendency of the myocardotic to wind up sooner or later with severe coronary artery disease. It is vital indeed to recognize early the vague symptomatology that makes up the myocardosis syndrome for only in this way can we initiate treatment which will give a longer span of life to these patients.

Case 1. H. G., a man, aged 30, physician, native of the United States. He was first seen by me in August 1931, with chief complaints of mild precordial pain, slight dyspnea on exertion and some palpitation when tired. The family history was noteworthy because of a familial tendency to coronary occlusion. His past history was negative except for several attacks of tonsillitis for which a tonsillectomy had been done, mild grippe a few years prior to his first visit, and an appendectomy in 1929.

His symptoms had been present for several years; however, the precordial pain, dyspnea and palpitation had become somewhat more prominent, though these were still far from severe. For the last few months he also experienced several mild attacks of indigestion which were promptly relieved by alkaline powders.

Upon physical examination the patient did not appear ill. He was 5 feet ten inches tall, weighed 156½ lbs., and his blood pressure registered 140 systolic and 100 diastolic. The examination was entirely negative. His vital capacity, standing, was 4,600 c.c., and he was able to hold his breath for 46 sec. The urine, blood count, blood sugar and blood urea were all normal; blood Kahn-Wassermann, negative.

Fluoroscopic examination showed slight aortic widening and some increased hilar markings.

The electrocardiogram showed a normal mechanism with no evidences of myocardial damage. (Figure 1.)

Subsequent Course: In spite of the negative findings and the youth of the pa-

tient, because of the characteristic symptom, and in view of the family history, a diagnosis of myocardosis was made. The patient was advised to rest every afternoon, to discontinue night and early professional calls, and to ease up mentally. Being a true disciple of Aesculapius, he did none of these things and continued to work hard and long.

Three years later, in July 1934, he experienced a severe attack of coronary thrombosis and was attended by another physician for several weeks. His convalescence was uneventful and the electrocardiograms taken six weeks following

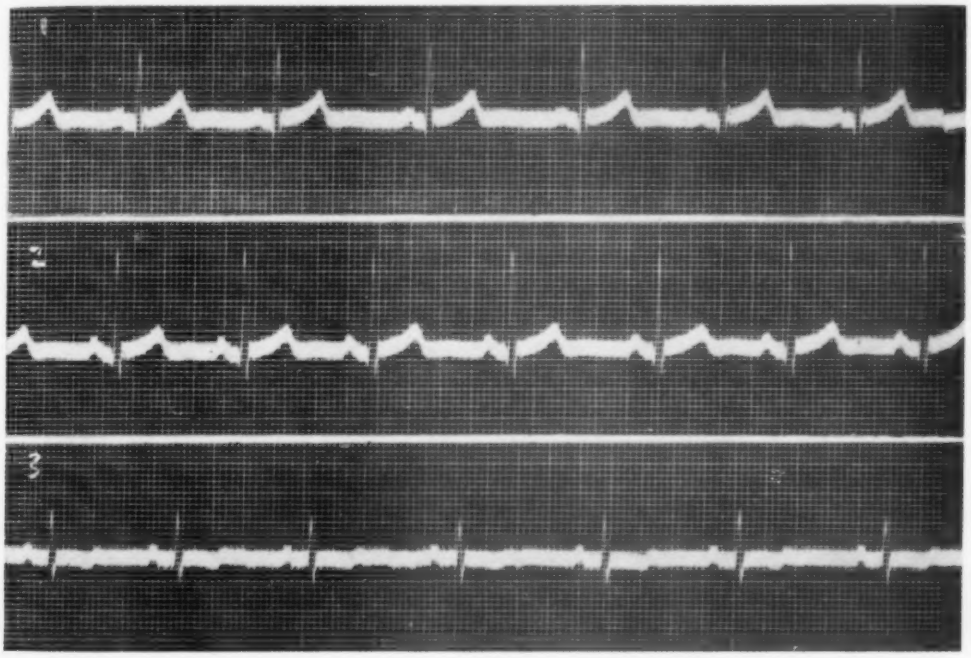

FIG. 1. The first electrocardiogram in Case 1; normal mechanism with no evidence of myocardial disease.

the attack showed the typical changes so often found after a severe coronary occlusion with subsequent infarction. (Figure 2.)

Note the inverted T-waves in Leads II and III, and the marked left axial rotation. Compare this with the first tracings taken three years before.

Another tracing taken four months following the occlusion showed the T-wave in Lead II less sharply inverted, but T_3 unchanged. (Figure 3.)

After this attack, as is so often the case, the patient complained much less of precordial discomfort, but the palpitations and dyspnea were still present.

This case is a clear example of the myocardotic who refuses to ease the strain on his myocardium and so hastens the final stage of the breakdown, namely, coronary occlusion. It is also worthy of emphasis that vigilance must not be relaxed because the patient happens to be in his thirties. Middle age, after all, is not only a matter of chronology, but varies markedly with the individual.

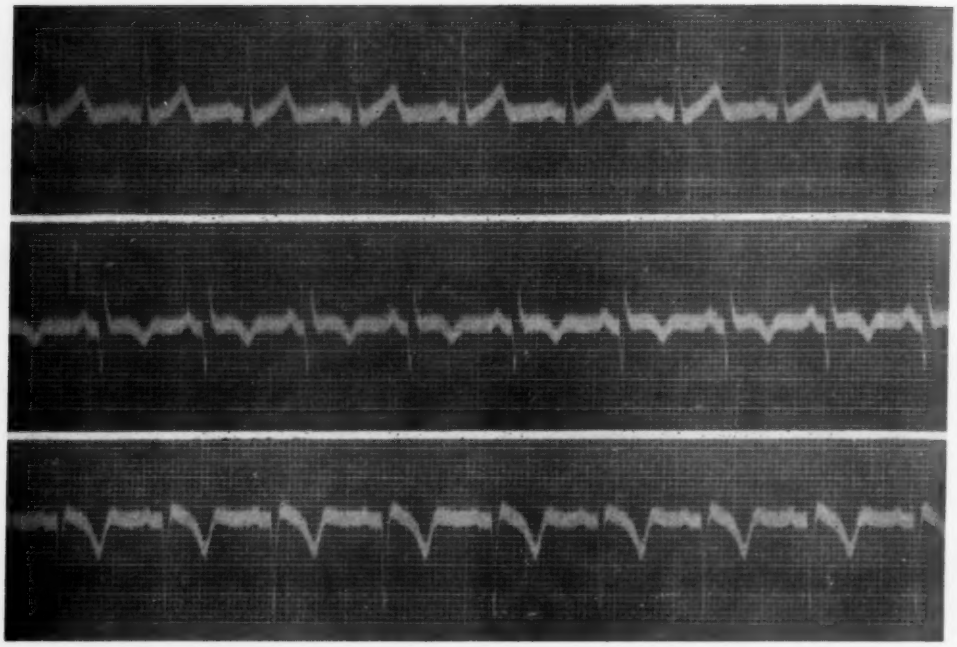

FIG. 2. Electrocardiogram in Case 1 six weeks after the attack of coronary thrombosis.

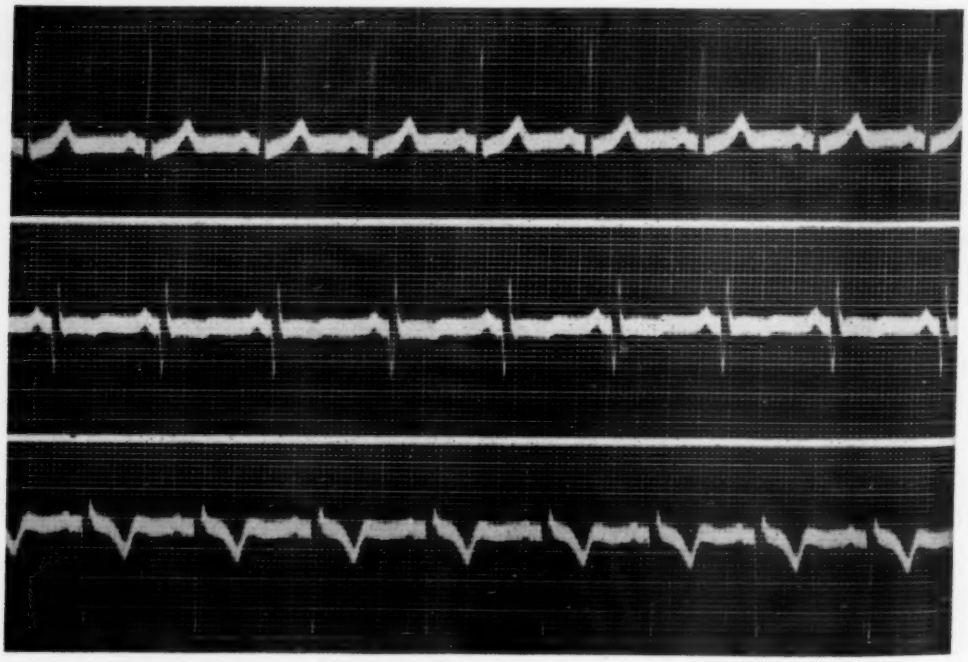

FIG. 3. Electrocardiogram in Case 1 four months after the attack of coronary thrombosis.

Case 2. S. K., a man, aged 55, upholsterer, native of Russia. He was first seen by me in July 1928, with a chief complaint of pain over the precordium; this was cramp-like in character and of three weeks' duration. Upon walking, the patient experienced a sensation of tightness around the upper chest, which would be promptly relieved by a short rest. Several months ago he had a similar sensation while in bed. Of late he was also conscious of increasing dyspnea upon exertion.

Family and past medical histories disclosed nothing of importance. Routine physical examination, laboratory, fluoroscopic and electrocardiographic studies at this time were entirely negative. His blood pressure registered 130 systolic and 70 diastolic.

Subsequent Course. In view of the patient's age group, characteristic history, yet negative findings, a diagnosis of myocardosis was justifiable, the patient so treated and followed up.

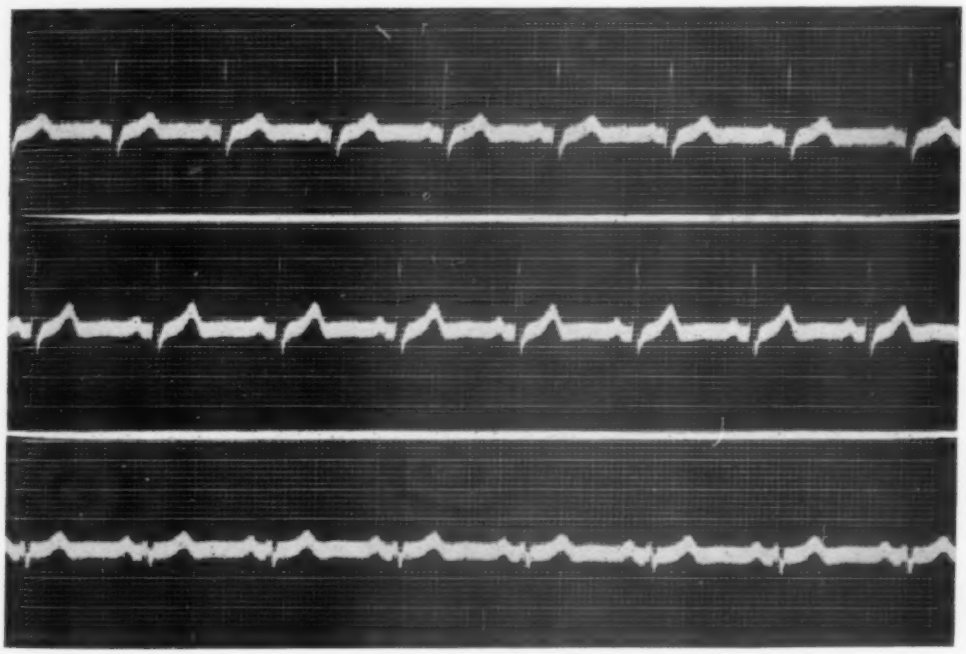

FIG. 4. Electrocardiogram in Case 2 prior to his attack of coronary thrombosis.

In 1932, he began to complain of vague gastric symptoms in the typical myocardosis fashion. Electrocardiographic studies at this time were also entirely negative. (Figure 4.)

In 1933, when the patient was 60 years old, he had a typical attack of coronary occlusion. The electrocardiograms taken some weeks after the seizure show the usual findings in such cases, as seen in figure 5.

This case is illustrative of the myocardotic in the usual age group with the fairly characteristic chain of events. It may be pointed out here that there was a lapse of five years between the myocardosis symptomatology and the first coronary occlusion.

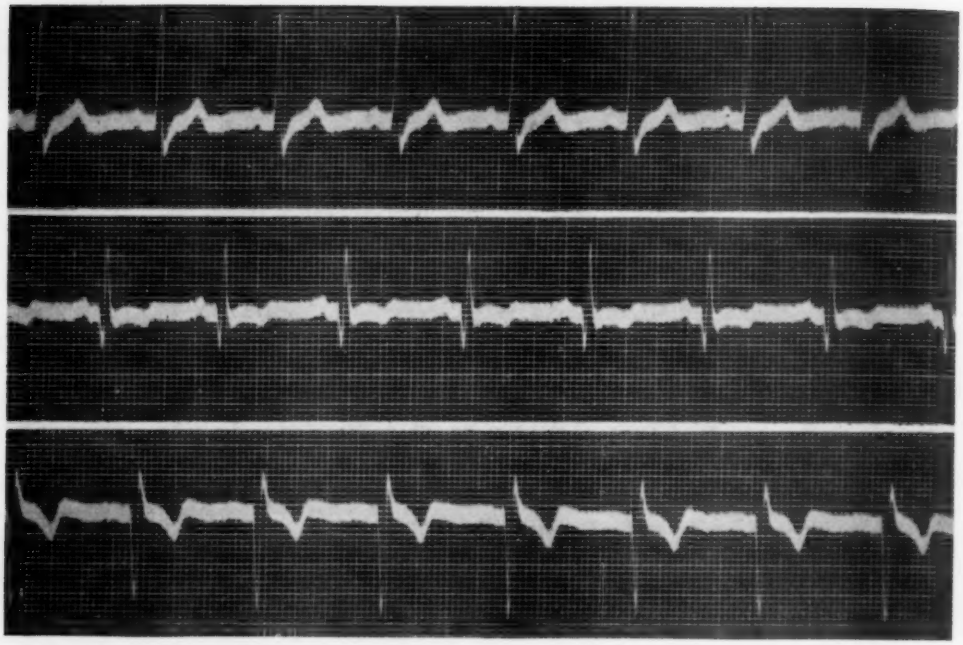

FIG. 5. Electrocardiogram in Case 2 subsequent to his attack of coronary thrombosis.

Case 3. D. J. R., a man, aged 43, silk manufacturer, native of the United States, was seen by me for the first time in August 1932, with the chief complaints of heartburn and eructations. These symptoms began as a vague gastric discomfort accompanied by belching after meals about three years prior to his first visit. The symptoms would become aggravated after a day of hard work. Substernal pressure after effort made its appearance shortly thereafter. With rest the latter disappeared quickly. Of late, however, the gastric symptoms were becoming more troublesome, so that he finally went to his doctor for relief.

Except for a ruptured appendix with peritonitis, his past history disclosed nothing of importance. His father had died of apoplexy at 58, and his mother of kidney disease at 74.

The findings upon physical examination were entirely negative; blood pressure registered 140 systolic and 85 diastolic, vital capacity, standing, 3,500 c.c., breath holding test, 55 seconds. Urine, blood count, blood chemistry and blood Wassermann were all negative.

The electrocardiograms showed a normal mechanism with no axis deviation and no inversions of the complexes in Leads I and II; Lead III showed negative P-waves, diphasic QRS complexes and bizarre T-waves with a moderately high take-off. There was a somewhat deepened Q-wave. Interpretation: Myocardosis, early evidence of coronary changes. (Figure 6.)

Subsequent Course. The patient received the usual advice and treatment and was told to report at a future date. He was last seen in April 1934, five years after the onset of his original symptoms. At this time he was complaining of some pains in the neck and left shoulder upon exertion, a symptom which is so common in the advanced stages.

This case demonstrates very clearly another type of myocardotic, whose chief complaints are gastric rather than cardiac, so aptly named by Riesman

"gastric masquerade." [24] These symptoms had been present for three years before the patient considered them of sufficient importance and annoyance to consult his doctor. The true cardiac symptom of substernal distress was only elicited by a careful system review and close questioning. By the time this man was first seen he could no longer be considered as fitting into the early myocardosis group. He was much further advanced along the sclerotic road and was showing unmistakable electrocardiographic evidences of myocardial damage.

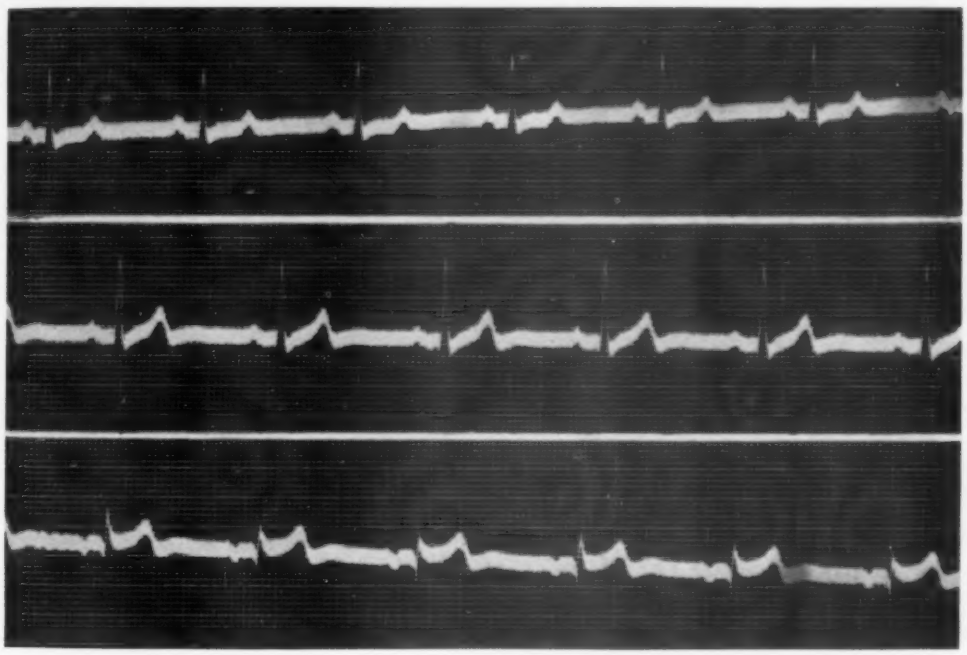

FIG. 6. Electrocardiogram in Case 3 showing changes indicative of early coronary disease.

Case 4. A white woman, aged 33, saleswoman, native of the United States. She was first seen by me in September 1930, complaining of a sensation of precordial discomfort, more marked on exertion. The patient's past history is interesting in that at the age of 16 she began to gain weight rapidly, so that at 33, though only five feet three inches in height, she weighed 210 pounds. She smoked cigarettes incessantly, ate inordinately and drank spiritous liquors more than a little. She was a very poor sleeper.

Her family history revealed a high incidence of deaths due to coronary occlusion. The girl felt that all her symptoms were caused by her excessive smoking and lack of sleep. Her physical examination, however, at this time was entirely negative, except for the overweight factor.

Subsequent Course. In view of the significant family history, in spite of the fact that this might have been considered a "tobacco angina," I felt that this was another example of early myocardosis and should be carefully followed. However, in typical fashion, the patient disappeared for a space of three years.

When seen again at the age of 36, she had an increased sense of precordial

discomfort, moderate dyspnea and some palpitation. She now smoked between 80 and 100 cigarettes daily, and took phenobarbital nightly in the effort to get some sleep. Physical examination, urine, blood count, blood chemistry and blood Wassermann were all negative. Her weight was now 197.5 pounds, and blood pressure 120 systolic and 70 diastolic. The electrocardiograms showed a normal mechanism with tendency to right axial rotation. (Figure 7.)

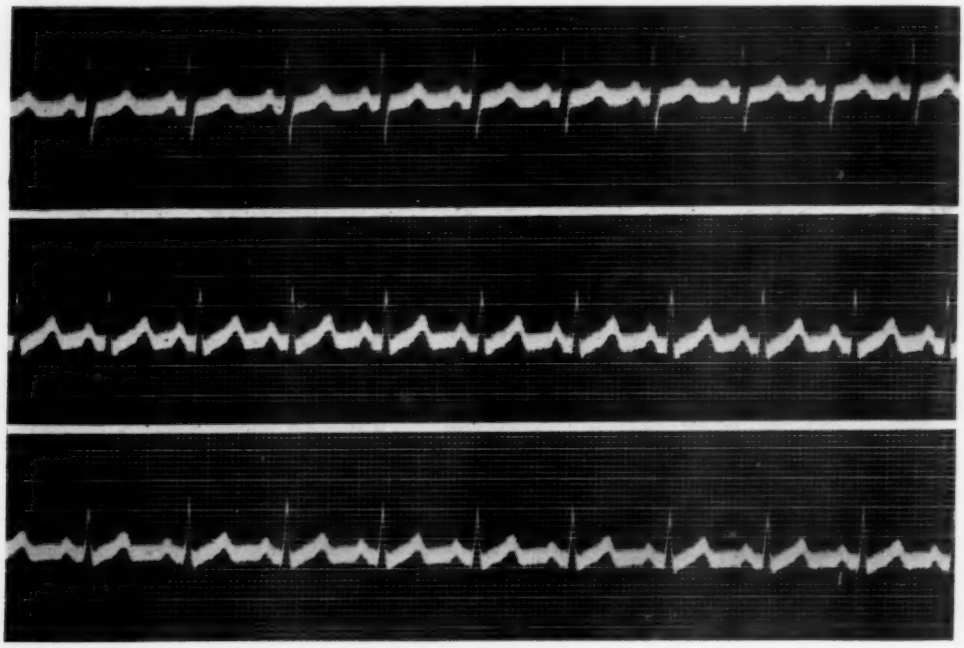

FIG. 7. The first electrocardiogram in Case 4.

A year later she returned with a history of having had an attack of epigastric pain a month prior to her visit. The pain had been so severe that it had kept her in bed for several days. Examination at this time revealed marked dyspnea, cyanosis and scattered moist râles in both bases; there was no hepatic or splenic enlargement. Blood pressure registered 90 systolic and 70 diastolic. Heart sounds, though regular, were markedly subdued in tonal quality, but no murmurs, shocks, thrills or extrasystoles were noted. Fluoroscopically, the heart was of mitral configuration with definite left ventricular enlargement. Cardiac contractions were toneless and the diaphragmatic excursions were limited. Lung fields were clear.

The electrocardiograms showed the typical T-wave alterations of a coronary occlusion. (Figure 8.)

The patient was now experiencing daily attacks of pain radiating to both shoulders, arms and finger tips. She reported to the office more frequently because of the anxiety caused by the practically constant attacks of precordial pain, increasing dyspnea and palpitations. Her blood pressure varied between 90 and 120 systolic, 65 and 80 diastolic.

The last electrocardiograms obtained reveal the marked changes which were going on in the myocardium. (Figure 9.)

Suddenly, on the night of March 10, 1936, the patient had another severe attack of coronary occlusion and died.

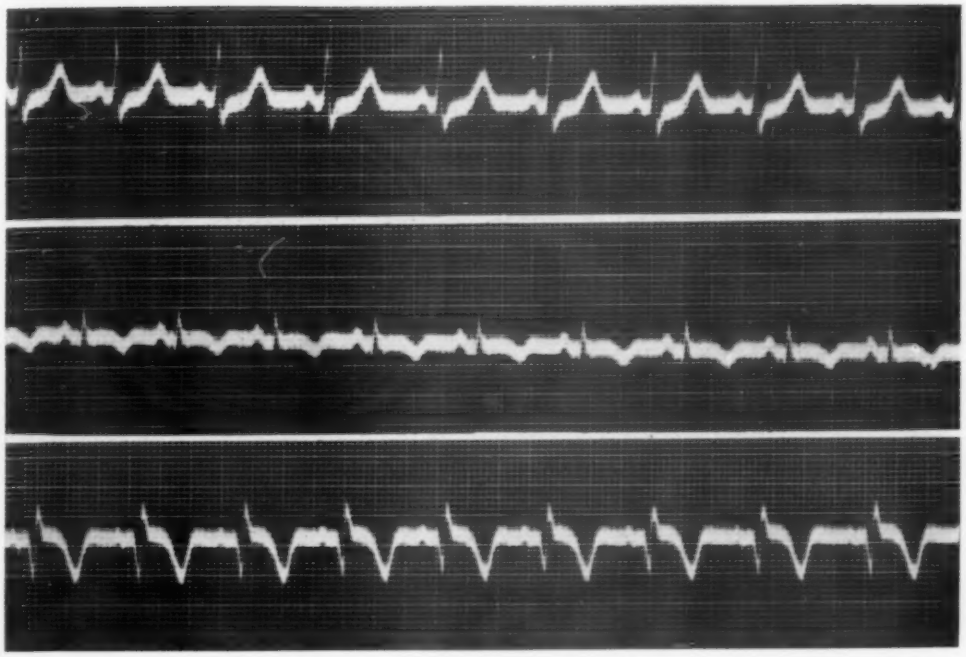

FIG. 8. The second electrocardiogram in Case 4 with evidence suggestive of coronary occlusion.

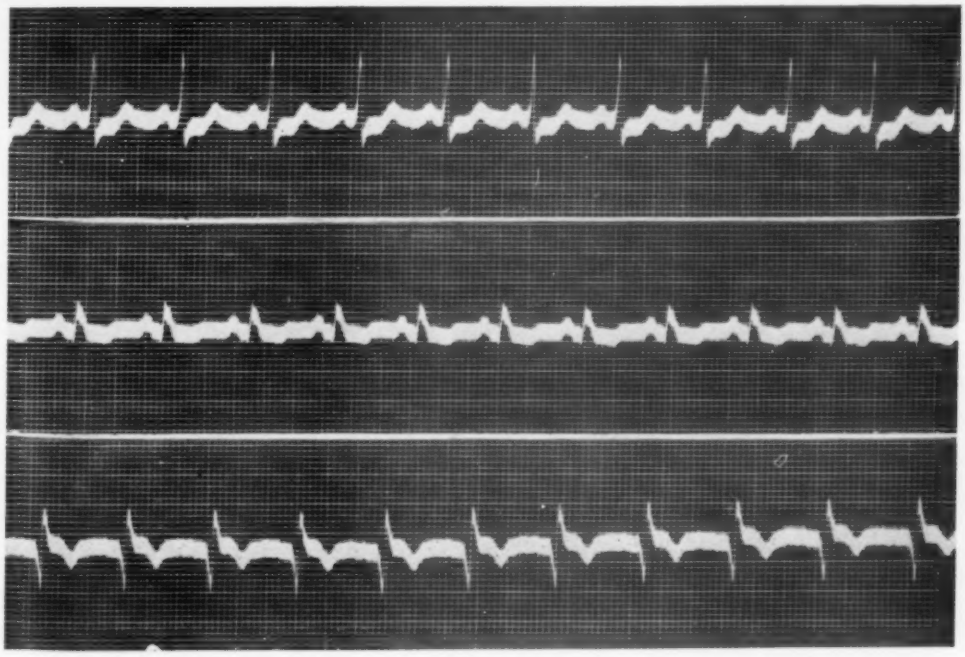

FIG. 9. The last electrocardiogram in Case 4, taken shortly before the patient's death from coronary thrombosis.

This case demonstrates very clearly that although " tobacco angina " may be found, great care must be taken to rule out myocardosis before daring to dismiss such a patient with the light admonition to stop smoking. The careful physician will detect these cases and carry them along for years if they coöperate, while the unwary will often let them pass undiagnosed, per haps to his subsequent confusion and embarrassment.

The man who has been trained to scientific doubt may feel that, though the cited cases seem to bear out our point very nicely, they may be exceptional. However, such instances are common and may be duplicated by any one who makes a serious effort to obtain an accurate history before arriving at a diagnosis.

In a paper by Phipps,[29] in which he discusses the early precursors of coronary thrombosis, the following interesting tabulation is given of the symptoms preceding coronary thrombosis:

Past History in 235 Cases of Coronary Thrombosis

Past History	Cases	Approximate Percentage
None	36	15
Angina or previous thrombosis	90	38
Dyspnea (only)	21	9
Paroxysmal nocturnal dyspnea	17	7
Myocardosis	47	20
" Sweating "	5	2
Indigestion	19	8

It is highly significant that 20 per cent of these cases of coronary thrombosis showed evidence of myocardosis before their attacks. Only " angina or previous thrombosis " surpassed myocardosis as an early symptom preceding the occlusion. Of further interest is the fact that the other underlying conditions given, either singly or in combination, are all met with in individuals suffering from myocardosis. These are " dyspnea (only)," and " indigestion." If such cases are combined with the myocardotics in Phipps' group the total would rise to the formidable figure of 37 per cent. Though Phipps [29] says:

> I am using the term ' myocardosis ' rather than ' stenocardia ' or ' arteriosclerotic heart disease ' for I believe that a more concrete symptom complex exists if it is restricted to cases presenting the triad of symptoms palpitation, dyspnea, and precordial discomfort or pain. . . .

I feel that unless the vaguer symptoms are included, many of the early cases will be missed.

This added evidence should convince the most skeptical of the definite relationship between myocardosis and coronary occlusion. Every physician should be able to recognize the myocardosis syndrome if he is willing to give his patient complaining of vague chest and gastrointestinal symptoms the time necessary to obtain a history in all its minutiae, and following this a careful physical check-up.

Summary

1. The need for a term to replace the incorrect "chronic myocarditis," has been stressed.

2. The peculiar aptness, both from a clinical and pathological point of view, of the term *myocardosis* has been shown.

3. The symptomatology of myocardosis has been discussed in detail.

4. The objective tests for the diagnosis of myocardosis have been given and their shortcomings pointed out.

5. The treatment of myocardosis has been outlined.

6. The fact that myocardosis is a precursor of coronary occlusion has been shown both by our own cases and by the statistics of others.

7. Finally, the fact is stressed that if we wish to prolong life in this group of patients, it is essential that every physician become familiar with the myocardosis syndrome, both in its frank form and its obscure types, so that he may regulate the patient's life at once in order to delay or, in rare instances, entirely prevent the ultimate coronary occlusion.

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PHYSIOLOGIC EFFECTS OF EXTENSIVE SYMPATHECTOMY FOR ESSENTIAL HYPERTENSION: FURTHER OBSERVATIONS *

By Edgar V. Allen, M.D., F.A.C.P., and Alfred W. Adson, M.D.,
Rochester, Minnesota

In previous communications we have presented our experiences with extensive sympathectomy for essential hypertension.[1-5] We are now reporting our experiences with a large number of patients and with the effects of operation on patients who have been observed over longer periods of time than were those of the earlier reports. We have continued to treat patients with essential hypertension by extensive sympathectomy for we are impressed with the fact that essential hypertension is in many instances an extremely serious disease for which medical treatment is far from satisfactory. Prosecution of this work, the aim of which was remedy or cure while there yet was possibility of either, opened the opportunity to determine the effects of the operation on blood pressure, symptoms and health, and to learn whether the surgical treatment modified the eventual mortality in essential hypertension. It also became possible to investigate the question of whether good results of operation are transient or permanent and whether or not patients could be selected so that more of them would benefit from operation.

The surgical treatment of essential hypertension is relatively new and the only way one can gain information about the results of extensive sympathectomy is to survey a relatively large number of patients. Such a survey will draw more sharply the distinction between patients who are suitable, and those who are unsuitable for operation.

The Technic and Rationale of the Operation

The technic used was that which Adson devised and which has been described in detail elsewhere [3]; it consists of bilateral subdiaphragmatic extraperitoneal resection of the splanchnic nerves, celiac ganglions and the upper two lumbar sympathetic ganglions. First the operation is performed on one side and then, about ten days later, on the opposite side. In addition, in the first 25 operations one-third to two-fifths of each suprarenal gland was removed. This procedure apparently did not offer any advantage or disadvantage over removal of only the other structures named.

It is known that in essential hypertension the fundamental cause of the elevation of blood pressure is the increase in the resistance offered to the

* Read before the meeting of the American College of Physicians, New York, April 5, 1938.

From the Mayo Clinic, Rochester, Minnesota.

flow of blood through the peripheral parts of the arterial system. Whether this increased arteriolar resistance is attributable to some inherent quality of the arterioles themselves, whether it results from some as yet undetermined substance circulating in the blood stream or whether it results from vasomotor stimuli transmitted from intracranial centers to the arterioles, or to all these, or other factors, cannot be stated definitely. The operation of sympathectomy for essential hypertension is based chiefly on the presumption that the increased arteriolar tone can be released by operation on the sympathetic nervous system, thus lowering blood pressure. To explain good effects of operation on blood pressure it is not necessary to assume that stimuli transmitted over sympathetic nerves are responsible for increased arteriolar tone but only that sympathectomy may relieve increased tone. That arteriolar tone can be diminished by sympathectomy is well established clinically, by experience in the treatment of such conditions as Raynaud's disease and thrombo-angiitis obliterans. From study of patients with essential hypertension, it is apparent that there is no single basis for increased arteriolar resistance in essential hypertension. This observation is borne out in a study of the results of extensive sympathectomy for essential hypertension, for were the increased arteriolar tone owing entirely to stimuli transmitted over the sympathetic nervous system, extensive sympathectomy should produce uniform decrease in blood pressure, provided an adequate part of the body were sympathectomized.

Extensive sympathectomy produces two other effects which may be of value in the treatment of essential hypertension, namely, increase of the blood supply to the kidneys and prevention or diminution of the spontaneous liberation of epinephrine from the suprarenal glands. It is impossible to say, at present, whether the hypertension produced in animals by Goldblatt, by the procedure of diminishing the blood supply to a kidney, is comparable to essential hypertension of man, but on the assumption that it may be, extensive sympathectomy is designed to sympathectomize the kidneys and thus increase the blood supply to them. We believe that it is improbable that sympathectomy of the suprarenal glands, which is accomplished as part of the operation performed at The Mayo Clinic, is of value in any other way than by diminishing or excluding episodes of marked release of epinephrine from the adrenal glands. Whether extensive sympathectomy is more valuable in the treatment of essential hypertension than is supradiaphragmatic splanchnicectomy (Peet) or celiectomy (Crile) we do not know, but it is a more logical procedure for it relieves sympathetic control of the kidneys and the suprarenal glands as well as that of the intra-abdominal regions and that of a large portion of the lower extremities.

Method of Study

All of our patients were studied in the clinic and hospital before operation. Usually the maximal blood pressure occurred when they were ex-

amined at the clinic and were more nervous than they were in the quiet atmosphere of the hospital. In the hospital, 24 successive hourly determinations of the blood pressure were made so that the general level as well as the minimal blood pressure resulting from rest or sleep were ascertained. Determinations of the transverse diameter of the heart and thorax were made by measuring the shadow on roentgenographic films exposed at 6 feet (183 cm.). Electrocardiograms were made, urinalysis carried out and tests of renal function made by determination of the concentration of urea and sulfates of the blood and by clearance tests. The responses of the blood pressure to administration of 3 grains (0.2 gm.) of sodium amytal administered orally for three successive hourly periods and to the slow intravenous injection of a 5 per cent solution of pentothal sodium were determined in many cases. Following operation numerous determinations of blood pressure were made. Only a few of our patients were examined at the clinic after final postoperative dismissal but their home physicians cooperated by sending to us reports of the maximal blood pressure, as determined in the office, and of that determined after periods of rest of as long as 25 minutes. In all our tables where readings of blood pressure are noted subsequent to dismissal from the hospital, the figures are those sent us by home physicians and differ from preoperative determinations chiefly in that the minimal pressures noted are not those resulting from sleep and several hours of rest but only from a few minutes of rest. Information relative to effect of operation on symptoms also was obtained by questionnaire.

Mortality

Three hundred and eleven operations have been performed on 156 patients by neurosurgeons at The Mayo Clinic, without an operative death. In one case acute gangrenous cholecystitis developed following the first stage of sympathectomy and the patient died 10 days after operation on the gallbladder. Information relative to blood pressure and general health following postoperative dismissal from the hospital has been secured in 124 instances and these form the basis of this report. Since this study was completed, seven additional patients have been heard from; the results of operation paralleled roughly those in the 124 cases which form the basis of the tabulated results in this study. Seven patients have died subsequent to operation but not as a result of it (table 1). The knowledge which we have now, relative to selection of patients for operation, indicates that patients numbered 12, 3, 4, and 5 were distinctly not good candidates for operation, since their diastolic blood pressures did not decrease sufficiently in the direction of normal as a result of rest in bed. None of these patients would be operated on today. Case 7 was on the borderline. The level to which the blood pressure decreased as a result of rest was not sufficiently low to allow prediction of a good result and not so high that a poor result

TABLE I

Deaths Following Operation but not Resulting from It

Case	Age, years	Hypertension		Death; months after operation
		Group	Minimum*	
1	36	2	170/115	24
2	21	3	160/124	15
3	17	4	205/180	7
4	53	3	140/130	6
5	49	3	184/120	4
6	48	3	132/90	2
7	41	2	160/110	7

* Of 24 hourly determinations.

of operation could be predicted. In case 6 the patient's blood pressure responded adequately to rest and to intravenous injection of pentothal sodium (140 mm. of mercury systolic and 110 diastolic or, to use the brief method of expression that will be employed subsequently, 140/110[6]), and her death two months after operation as a result of a cerebral hemorrhage was not anticipated from preoperative studies.

Cerebral vascular accidents have affected two patients. The first patient, aged 48 years, whose blood pressure was of group 2 and whose minimal blood pressures preoperatively were 160/110 suffered a cerebral vascular accident 18 months after the operation; the surgical procedure had not influenced the blood pressure permanently. The other patient, who was 48 years of age and whose hypertension was of group 3, had a minimal blood pressure before operation of 160/90 and sustained a cerebral vascular accident 23 months following the operation; again the surgical procedure had not influenced the blood pressure permanently.

EFFECT OF OPERATION ON BLOOD PRESSURE AND PULSE RATE WHEN PATIENTS STAND

Decrease in the blood pressure and increase in the rate of the pulse when the patient changes from the recumbent to the upright position occurs commonly following operation (table 2). Earlier in our experience with the surgical treatment of hypertension we felt that these reactions gradually disappeared.[5] We can state now with finality that both orthostatic hypotension and orthostatic tachycardia disappear at variable times after operation, regardless of the effect of operation on the blood pressure. We do not know the explanation of this disappearance of orthostatic changes in blood pressure and pulse rate. It suggests that there is a regaining of arteriolar tone some time after operation but if this were true, good results of operation should not persist, which they commonly do. Further study of this problem is needed.

TABLE II
Effect of Upright Posture on Pulse Rate and Blood Pressure Following Operation *
(Ten Illustrative Cases)

Blood pressure				Pulse rate			
Before operation		After operation		Before operation		After operation	
Lying	Standing	Lying	Standing	Lying	Standing	Lying	Standing
220/110	200/110	170/95	80/50	112	104	84	120
198/116	200/126	160/106	140/102	94	108	80	124
154/110	148/112	134/94	128/90	80	116	76	120
150/108	160/114	128/92	110/92	72	124	88	115
168/114	182/130	158/110	118/92	88	120	120	156
182/116	164/120	140/112	118/92	80	92	92	124
200/110	192/120	192/110	148/116	84	100	92	138
162/110	162/122	194/122	94/78	84	108	88	120
210/138	208/146	178/118	70/40			100	138
200/130	165/120	136/100	114/80			84	121

* Two to three weeks following operation.

THE EFFECT OF OPERATION ON THE RESPONSE OF BLOOD PRESSURE TO A STANDARD STIMULUS

It is known that the blood pressures of patients with essential hypertension increase unusually as a result of immersion of a hand in ice water.[12] When the effects of operation on the blood pressure are minimal, the response of it to immersion of a hand in ice water is not significantly changed.[5] When the effects of operation on the blood pressure are good, the response of it to immersion of a hand in ice water is greatly diminished.[5] Thus, when the results of operation are satisfactory there is not only a general lowering of the blood pressure but a levelling off of the peaks which occur so commonly in essential hypertension.

THE EFFECT OF OPERATION ON SYMPTOMS

It has been commented on previously that the effect of operation on symptoms does not parallel the effect on blood pressure.[5] The results of operation on symptoms in this series of cases are presented in table 3. The

TABLE III
Effect of Operation on Symptoms

Symptoms	Per cent relieved		
	Poor*	Fair*	Good*
Headache	76	80	100
Nervousness	67	66	80
Pain in thorax	60	75	90
Fatigue on exertion	50	44	41
Dyspnea on exertion	48	46	50

* These designations refer to effect of operation on blood pressure.

percentage of patients relieved * of headache, when the effects of operation on the blood pressure were good, fair or were recorded as failure or temporary, were 100, 80 and 76 respectively. Nervousness was relieved after operation, when the effects of operation on blood pressure were good, fair or poor respectively in 80, 66 and 67 per cent of the cases. The percentage of patients relieved of non-anginal pain in the left side of the thorax after operation, when the effects of operation on the blood pressure were good, fair or poor were 90, 75 and 60 respectively. These figures bear out in a striking manner isolated clinical observations that patients are frequently relieved of such distressing symptoms as headache in spite of the fact that their blood pressure does not seem to have been significantly lowered. The explanation for this is not apparent. It may be that while we have considered the effects of operation on the blood pressure to be poor, the blood pressure has been reduced just enough in its general level, or at various times of the day, to prevent the occurrence of symptoms, or it may be that there is a psychotherapeutic effect of operation, such as Buck has demonstrated in treating patients without operation. Whatever the explanation, the results are unequivocal and on several occasions patients have stated that the relief of symptoms alone had justified the surgical procedure. In contrast to the relief of headache, nervousness and pain in the left side of the thorax, is the frequent failure of the surgical procedure to relieve such symptoms as fatigue and dyspnea with exertion. When the results of operation on the blood pressure were good, fair or poor, fatigue was relieved in 41, 44 and 50 per cent of instances respectively. In many instances patients noticed that fatigue with exertion after operation was significantly greater than it was before operation. When the effects of operation on the blood pressure were good, fair or poor, relief of dyspnea occurred in 50, 46 and 48 per cent of instances respectively. In many instances patients noted that dyspnea on exertion was greater following operation than it was before operation. The explanation for the frequent occurrence of increased fatigue and dyspnea with exertion after operation is not clear and more study of this problem is necessary. One patient, a physician, who noted both dyspnea and fatigue as a result of exertion following operation, noted marked decrease of his blood pressure and acceleration of the rate of his heart as a result of exertion. None of the patients has been disabled by these symptoms but all have carried on activity in a normal manner or somewhat reduced activity. Both dyspnea and fatigue with exertion tend to disappear as the time after operation increases.

Effect on Sweating

Since removal of the first and second lumbar ganglia interrupts the sympathetic pathways to the lower extremities, the function of sweating of

* The term "relief" indicates significant amelioration as well as complete disappearance of symptoms.

the lower extremities is eliminated. The level at which sweating ceases is variable. Most commonly there is no sweating distal to the midthigh area after operation but occasionally the level of cessation of sweating is at the knees or as high as midway between the umbilicus and the symphysis pubis. Since there is some anatomic variation of distribution of sympathetic fibers, the area from which sweating is eliminated is not always the same on both sides following operation.

The Effect on the Heart

When operation produces good results on blood pressure, T-waves that originally were inverted in the electrocardiogram may become upright and the transverse diameter of the heart, demonstrated on roentgenographic films exposed at 6 feet (183 cm.) may decrease. Tachycardia occurs commonly when the patient stands or exerts himself following operation but this reaction gradually disappears. We have not had a sufficient number of patients return for reëxamination following operation to allow us to state how commonly significant electrocardiographic changes persist or how frequently there is significant reduction in the transverse diameter of the heart.

Illustrative Case. A man, aged 34 years, was examined at the clinic in January 1936. Hypertension had been present for three years and the patient complained of headache and fatigue. There had been a gradual increase in the blood pressure. The blood pressure ranged from 214 systolic and 140 diastolic to 145 systolic and 100 diastolic. The mean values were 170 for the systolic pressure and 120 for the diastolic pressure. The transverse diameter of the thorax was 30 cm. The greatest transverse diameter of the heart was 14.5 cm. and an electrocardiogram revealed inverted T-waves in Leads I and II. Urinalysis disclosed albuminuria, grade 2. The patient had retinitis; examination of the ocular fundi revealed narrowing, grade 1, and sclerosis, grade 2, of the arteries. Extensive sympathectomy was performed on January 22 and on February 12, by using the technic described by Adson.

The patient returned to the clinic for reëxamination four months after the last operation. At that time the blood pressure ranged from 114 systolic and 80 diastolic to 110 systolic and 80 diastolic. The mean values were 112 for the systolic pressure and 80 for the diastolic pressure. The transverse diameter of the thorax was 28 cm. and the greatest transverse diameter of the heart, 12.5 cm. Electrocardiographic examination did not reveal inversion of the T-waves. Albuminuria had disappeared and the value for blood urea was 28 mg. per 100 c.c. There was no evidence of retinitis. Narrowing of the retinal arteries remained the same as it had been but the sclerosis was of grade 1. Seven months after operation, the values which were determined at intervals of five minutes were 135, 130 and 130 for the systolic pressure and 100, 98, and 102 respectively for the diastolic pressure. The patient had dyspnea, grade 1, but the headache had disappeared, and his strength was 80 per cent of normal. Twenty-four months after operation, the blood pressure was normal and the patient was entirely well.

In this case successful operation caused reduction in the transverse diameter of the heart and disappearance of inverted T-waves in the electrocardiogram as well as disappearance of retinitis and albuminuria.

Effect on Renal Function

Most of our patients who were operated on had no impairment of renal function; patients whose renal function was impaired were not operated on. Since we have not had opportunity to study the renal function of many of our patients a considerable time following operation and since tests for renal function when it is not significantly impaired are not always reliable for comparative purposes, we cannot say that renal function is improved following successful operation. The observation that it is improved, however, has been made by Freyberg and Peet. It is apparent that renal function is not impaired when blood pressure is greatly reduced by operation. This observation agrees with those of Freyberg and Peet, of Page and Page and Heuer. Diminution of the amount of albumin in the urine, or disappearance of it, occurs commonly following successful operation.

The Effect on Temperature and Motor Function of the Extremities

Following the operation the feet are warm and dry. If the blood pressure has been significantly decreased by operation the hands may be cold, apparently owing to vasoconstriction in these parts. An occasional patient noticed generally increased tolerance to warmth. The sensation and motor functions of the lower extremities were not impaired. A few patients mentioned an area of numbness, variable in extent in different cases; this is owing to section of, or traction on, the lateral branches of the eleventh and twelfth intercostal nerves at the time of operation.

Effect of Operation on the Retinas

This subject can be presented only incompletely here since complete data, which will be the basis of a subsequent report, have not as yet been assembled.

The changes following operation do not appear to be constant and cannot always be correlated with the effect of operation on the blood pressure. The retinas of patients who have been examined several months after operation and whose blood pressures have not been significantly influenced have not appreciably changed in appearance in most instances. In instances in which the blood pressure has been reduced by operation, retinitis may disappear and apparent sclerosis and arteriolar spasm may be greatly diminished. However, in spite of significant reduction in blood pressure, examination of the retinas may disclose changes of the same degree as those observed preoperatively.[9] Mild retinitis has been observed in a few instances when it did not exist preoperatively. The cause of improvement in the appearance of the retinas following operation is not entirely clear for reduction of blood pressure by extensive sympathectomy should not influence spasm of the retinal arteries (as sympathetic control of them is not impaired), unless

hypertension itself provokes arteriolar spasm or unless operation removes some mechanism which causes spasm. Again, if the results of the experimental work of Goldblatt on dogs can be transferred to human beings who have hypertension, it is possible that increase in the renal blood flow may cause generalized decrease in arteriolar tonus, thus relieving spasm of the retinal arteries. One might logically suppose that there would be more evidence of narrowing of the retinal arterioles or of retinitis after operation than before in cases in which the blood pressure was significantly reduced by operation, as the increased arteriolar tonus which is present in essential hypertension would be partially unopposed in this location as a result of reduction in blood pressure. In some instances we have noted that there is clinical evidence of diminished circulation to the hands following operation, manifested by coldness of the skin. This may result from partially unopposed arteriolar spasm occurring in a way in which it might be expected to occur in the retinas. The entire matter needs further clarification.

Effect of Operation on Intestines

Disturbances of intestinal function were noted in a number of instances. Periods of three to four bowel movements daily, with stools of soft consistency, alternated with periods of normal bowel movements. In many instances constipation was relieved. Flatulence or other evidence of disturbed motor activity of the gastrointestinal tract were uniformly absent.

Effect of Operation on Sexual Function

The sexual function of women is not impaired. Dysmenorrhea may be relieved. Menstruation is not influenced. Fertility is not affected apparently, although the response of the blood pressure to pregnancy is variable. In one case in which blood pressure was normal for many months after operation, toxemia of pregnancy with hypertension developed and hysterotomy was required. Immediately after operation the blood pressure returned to a normal level but several months later it again reached preoperative levels. Another patient, whose blood pressure had been normal for many months following operation, experienced an entirely normal pregnancy without elevation of the blood pressure or signs of toxemia of pregnancy and was delivered of a healthy child. Avoidance of pregnancy seems advisable ordinarily. Usually libido and potentia coeundi of the male are not impaired. However, some patients note diminished libido. Associated with orgasm, there is usually no ejaculation of fluid although some may pass into the urethra. Men may be sterile but are not certainly so.

Effect of Operation on Suprarenal Glands

Although partial suprarenalectomy was a part of the procedure in the first 25 cases of this series, Addison's disease never has been observed fol-

lowing operation. Significant changes in the amount of sodium and chloride in the blood have not been determined, regardless of whether the suprarenal glands were partially resected. However, increases in the amount of potassium, averaging 3 mg. per 100 c.c. have been observed in eight cases, in five of which partial suprarenalectomy was not performed.

Effect of Operation on Blood Pressure

As was expected, the effects of operation on blood pressure are not uniform. They vary from poor to excellent. Depending on the effects of operation on blood pressure we have divided our patients into four groups (table 4). In the group of patients, in treatment of whom results were

Table IV

Results of Operation on Blood Pressure

Results	Number of cases	Per cent
Failure*	25	20
Temporary†	35	28
Fair	35	28
Good	29	24

* Immediate effect on blood pressure inconsequential.

† In 7 instances good or fair results persisted many months. In 28 instances they persisted only from 2 to 8 months.

designated as " failures," the diastolic pressure was not very much reduced at the time of dismissal from hospital following operation. In many instances, however, there was considerable reduction in the systolic blood pressure, which indicates what has been observed on a number of occasions; namely, that the systolic blood pressure is more easily influenced by operation than is the diastolic blood pressure. As can be seen in a study of the results given in table 5, even in some instances in which we have considered the results of operation on the blood pressure to be poor, the systolic pressure has not reached its preoperative level. However, we consider the results of operation in this group of cases to be failures, since they were distinctly disappointing and since there is some question whether moderate reduction in the systolic blood pressure is of any great significance when the diastolic pressure is influenced but little or none at all.

Illustrative Case of " Failure." A woman, 48 years of age, knew she had had hypertension for seven years and complained of headache, fatigue, nervousness, pain in the left side of the thorax, dyspnea and dizziness. On examination she was found to have hypertension, with blood pressures which ranged between 250/114 and 190/95, and with mean pressures of 170/110. The heart was not significantly enlarged. The T-waves were diphasic in Leads II and III in the electrocardiogram. There was moderate sclerosis and narrowing of the retinal arteries and hemorrhages and exudates. The concentration of blood urea was normal. The urine contained albumin, graded 2. Following her second operation her blood pressures ranged from

200/130 to 180/100 with a mean pressure of 190/110. Two months following operation the blood pressures ranged from 210/130 to 188/120 and seven months following operation they ranged from 222/130 to 194/120. Seventeen months postoperatively the blood pressures ranged from 200/140 to 198/138. All her symptoms were originally benefited by operation but 17 months following operation the patient noticed return of pain in the left side of the thorax, and dyspnea, although relief of nervousness and headache had persisted. There were no significant lowerings of blood pressure at any time after operation.

The results of operation on a second group of patients have been designated "temporary" (table 4). This designation applies to a group of patients whose blood pressures were significantly lower following operation than they were preoperatively but whose blood pressures returned to approximately the preoperative level either between the time of dismissal of the patients from the hospital and our first subsequent record of their blood pressure (two to eight months), or whose blood pressure, which was originally significantly reduced by operation, returned to the preoperative level during the period when the patients' home physicians were sending us records of the blood pressure (cases 54, 55, 56, 57, 58, 59, 60 of table 5). In all cases of this group the blood pressure eventually returned to approximately the preoperative level.

First Illustrative Case of "Temporary" Result. A woman, 35 years of age, had known of her hypertension for two months. The only symptoms which she had noted were headache and fatigue. On examination she was found to have hypertension, with blood pressures which ranged between 210/130 and 150/105. Also, sclerosis and narrowing of the retinal arteries, retinitis, slight enlargement of the heart and inversion of the T-waves in the third lead of the electrocardiogram were present. Blood urea and serum sulfates were of normal concentration. Immediately following operation, the blood pressures ranged from 165/126 to 120/80 and six months following operation they ranged from 168/110 to 142/108. Fourteen months following operation the blood pressures ranged from 150/95 to 145/90. Headache and dyspnea had almost entirely disappeared. Twenty-one months following operation, however, the blood pressures ranged from 210/134 to 210/130. Twenty-nine months following operation they ranged from 176/160 to 220/140. Headache had returned and the patient complained of weakness and dizziness. Good effects of operation on blood pressure had persisted only from fifteen to twenty-one months.

Second Illustrative Case of "Temporary" Result. A woman, 31 years of age, had known for five years that she had hypertension. She complained of headache and pain in the thorax. On examination, the blood pressures were found to range between 220/142 and 140/100, with mean pressures of 180/110. There was moderate sclerosis of the retinal arteries. Electrocardiographic examination and estimation of the blood urea gave normal results. Immediately following operation the blood pressures ranged from 160/115 to 110/75, with mean pressures of 150/95. However, six months after operation they ranged from 180/122 to 162/120 and ten months after operation they were 175/130 to 165/125. Subsequently, there was further elevation of the systolic blood pressure. Fair results of operation on blood pressure had persisted only six months or less.

There were 35 instances of fair results (tables 4 and 6). In these there was significant reduction of blood pressure which, however, did not approach normal levels.

TABLE V

Effect of Operation on Blood Pressure: Failure, or Temporary Results

Case	Blood pressure			Months after operation
	Maximum	Minimum	Mean	
1	205/130 192/122 220/140	160/110 184/120 hemiplegia	180/125 188/120	18 24
2	190/140 218/146	130/100 210/142	180/130	28
3	210/145 210/150	170/115 195/150 dead	180/130	12 24
4	250/180	160/120 dead	*220/150 180/125	3 15
5	208/160 250/170 240/150	160/90 230/140 184/130	hemiplegia	8 23
6	220/140 180/122 205/145	140/100 160/120 210/135	180/110	5 21
7	230/140 200/130 205/145	190/115 200/120 188/140	200/126	3 19
8	240/160 170/122 230/160	210/110 148/108 245/145	220/130	2 17
9	240/190	205/180 dead		7
10	205/135 210/135 228/140	150/90 180/120 204/130		6 19
11	230/154 200/135	180/130 180/122	200/134 180/130	6 15
12	252/145	200/110	220/115 236/136	10
13	240/160 230/130	180/110 210/120	210/135 200/110	6 10
14	240/130 180/120	158/98 172/112	195/114	6
15	210/140 190/120 210/134	150/100 180/115 194/128	180/120	4 12
16	188/124 250/140 182/116	142/102 220/130 176/108	170/110 *	3 12
17	220/160 dead	140/130	190/145 180/120	6
18	200/140 220/140 224/136	164/100 200/138 184/134	172/120	3 11
19	224/126 212/118 230/130	160/100 200/116 220/118	180/110	2 8
20	230/140 184/128 210/140	168/112 180/118 178/134	180/124	2 7
21	220/156 210/130	150/90 200/120	170/110	8
22	230/140 184/126 220/140	178/108 184/126 200/130		2 7
23	250/130 240/130 255/150	180/100 220/130 235/145	215/115	2 5
24	230/148 180/140	150/100 180/115	170/120	7
25	240/160	184/120 dead	200/140	4
26	240/135 224/?	160/90 200/108	190/120	9
27	220/140	156/90	188/136 210/125	8
28	230/160 210/130	146/88 200/128		5
29	230/130 240/130	136/90 205/110	170/110	6

* Taking potassium thiocyanate.

TABLE V—*Continued*

Case	Blood pressure			Months after operation
	Maximum	Minimum	Mean	
30	214/140 212/134	170/104 210/124	185/125	6
31	178/130 216/126	128/80 196/120		6
32	225/160 204/140	170/110 194/120	190/125	6
33	200/140 190/125	110/50 178/120	190/120	5
34	215/140 240/148	155/110 190/140	180/110	5
35	220/160	150/110	200/140 210/140	3
36	244/172 188/122	135/110 180/120	178/120	4
37	220/150 190/130	120/95 160/108	180/125	3
38	245/160 190/140	190/125 160/120		3
39	185/130 270/135	132/90 dead	170/110	2
40	240/160 225/170 230/160	210/110 225/160 245/145	220/130	8 17
41	196/120 250/140	145/90 246/136	170/105	7
42	220/130 220/130 228/140	170/120 208/128 220/130	195/125	5 14
43	230/138 220/120 264/130	170/100 244/120	180/110	3 8
44	200/148 180/140	170/90 155/130		10
45	260/150 245/140	190/110 180/120	210/115	8
46	220/140 220/160	165/105 190/120		6
47	235/120 200/120	175/110 160/115	170/115	25
48	175/120 164/124	140/95 160/110		16
49	210/130 196/118	170/120 190/118		12
50	210/150	160/110 dead	180/130	7
51	210/132 210/120	170/100 198/118	190/120	2
52	215/150 214/150	170/115 210/140	190/125	2
53	230/150 200/?	170/105 186/?	190/125	2
54	210/130 150/95 220/140	150/105 140/95 180/160		8 23
55	260/160 162/108 216/156	180/120 160/104 180/144		17 28
56	220/140 168/102 190/134	140/105 146/102 178/124	180/120	11 28
57	230/136 156/110 190/130	170/110 140/102 180/124	190/120	14 22
58	260/140 174/104 230/120	200/120 172/100	235/135	2 13
59	220/136 150/110 180/140	150/100 145/105 170/130	170/120	5 10
60	210/130 180/108 192/140	168/100 178/108 158/120	190/120 180/130	6 12

Illustrative Case of Fair Results. A woman, 23 years of age, had known for 14 months that she had hypertension. Her symptoms were dyspnea, nervousness and headache. At the time of examination her blood pressures ranged from 220/155 to 180/115, and the mean pressures were 200/120. There was some narrowing of the retinal arteries but no sclerosis. Retinitis was absent. Blood urea and sulfates were of normal concentration and the heart was not enlarged. Twelve months after operation the blood pressures ranged from 190/130 to 188/114 and 20 months after operation they ranged from 180/110 to 150/90. Headache had not been relieved but nervousness had lessened. There had been significant reduction of the blood pressure but the patient still had moderate hypertension.

Of the fair results there were four instances in which results of operation, which were originally good, became only fair eventually (cases 32, 33, 34 and 35 of table 6).

Illustrative Case of Fair Results Which Originally Were Good. A woman, 33 years of age, had known for nine years that she had hypertension. She complained of severe headaches and marked dyspnea and fatigue. Her blood pressures ranged from 205/135 to 140/100 with a mean pressure of 160/110. Marked narrowing and moderate sclerosis of the retinal arteries were present. Retinitis was evident. The concentration of serum sulfates was normal and T-waves were inverted in Leads II and III of the electrocardiogram. Five months after operation the blood pressures were 145/100 on several occasions. In the next 16 months three reports indicated that the blood pressures had not increased. However, 24 months after operation the blood pressures averaged 168/114 and 30 months after operation three consecutive readings, made in an office while the patient was resting for 25 minutes, were 170/110, 180/118 and 170/110. In this case the immediate good effects of operation on blood pressure were only fair 24 months after operation.

In 29 cases the results of operation on the blood pressure were good (tables 4 and 7). The eventual blood pressures were not within the range of normal in all of these instances but they were greatly reduced when compared with the preoperative readings.

Illustrative Case of Good Results. A woman, 31 years of age, had known for three years that she had hypertension. She complained of headache, fatigue, thoracic pain and dizziness. Her blood pressures ranged from 190/135 to 140/90 and the mean was 160/114. There was moderate sclerosis and narrowing of the retinal arteries but no retinitis. The heart was not enlarged, the concentration of blood urea and sulfates was normal and the electrocardiogram was normal, except for inverted T-waves in Lead III. Eight months after operation the blood pressures ranged from 126/98 to 118/82. Similar values for blood pressure were reported 15 to 18 months after operation. Twenty-three months after operation the patient's home physician reported the following readings taken in the office at intervals of five to ten minutes: right arm; 110/85, 84/66, 74/52, 74/54; left arm; 135/85, 114/92, 112/90, 112/90 and 120/94. The patient had gained 20 pounds (9 kg.) and all her symptoms had disappeared except fatigue, which persisted. In this instance good effects of operation on blood pressure have persisted 23 months.

Effect of Various Factors on the Result of Operation

Sex did not significantly influence the effect of operation on blood pressure, although a slightly higher percentage of women received good or fair

TABLE VI

Effect of Operation on Blood Pressure: Fair Results

Case	Blood pressure			Months after operation
	Maximum	Minimum	Mean	
1	220/155 180/110	180/115 150/90	200/120 170/100	20
2	240/105 190/100	135/90 162/90	178/98	26
3	210/140 174/122	130/75 160/114	166/118	17
4	228/142 180/115	170/108 175/112	200/120 188/114	15
5	205/130 195/?	130/90 178/?		17
6	200/130 170/120	140/100 160/115	160/120	2
7	200/138 180/120	138/90 175/115	180/110	2
8	180/120	130/90	170/110	8
9	220/140 176/118	140/90 176/118	160/110 176/118	7
10	220/140 188/114	122/80 174/108	170/110	4
11	225/130 186/124	130/70 164/110	160/100	6
12	210/150 176/100	150/100 166/100		7
13	230/125 186/100	150/100 150/98	170/115	5
14	230/122 198/120	160/100 186/102	190/110 190/108	7
15	188/120 180/114	140/100 156/102	164/108	5
16	234/140 185/112	165/108		3
17	212/128 162/118	160/110 142/100	190/120 148/106	4
18	210/140 168/120	140/90 145/115	190/115	5
19	186/120 170/120	145/94 130/104	160/104 150/106	4
20	200/130 176/106	140/90 170/100		5
21	224/140 178/112	170/112 160/108		5
22	268/140 164/120	170/100 154/110		4
23	230/160 180/120	180/112 158/108	200/130	20
24	190/120 170/110	130/90 162/108	160/105	6
25	204/132 172/110	170/100 166/108	180/114	6
26	224/142 190/?	145/125	185/130	3
27	224/140 178/112	170/112 156/108		5
28	268/140 164/120	170/100 154/110		4
29	184/118 180/110	130/90 156/90		4
30	230/140 186/120	180/100 180/108	215/120	3
31	190/130 166/110	130/100 164/108	160/115	2
32	205/135 150/100 160/96 210/146	140/100 130/100 150/90 170/110	160/110 180/120	12 22 31
33	225/130 128/90 142/82 190/120	150/100 126/84 138/80 140/106	190/110 170/110	9 20 26
34	210/168 146/102 170/120	168/110 144/100 160/120	180/120 164/120	10 17
35	230/140 160/110 180/125	140/85 146/102 158/110	160/110 170/120	9 20

TABLE VII

Effect of Operation on Blood Pressure: Good Results

Case	Blood pressure			Months after operation
	Maximum	Minimum	Mean	
1	190/135 150/100 135/85	140/90 135/100 112/90	160/114	15 23
2	180/114 150/92 154/100	144/90 150/90 150/90	174/110	13 26
3	240/140 135/102 155/105	145/100 130/98 140/95	170/120	8 23
4	220/150 150/106 142/104 160/110	170/120 128/90 140/100 144/108	190/130	6 12 23
5	220/120 152/92 172/110	140/100 150/88 132/80	180/110	4 23
6	205/120 168/100 170/100	175/90 168/95 165/100	200/110	10 18
7	200/135 122/86 140/100	150/90 112/78	180/114	2 5
8	235/160 150/90 150/100	180/98 120/80 118/50	210/130	3 9
9	220/140	146/78	175/100 140/?	3
10	210/130 158/90 164/98	152/95 156/88 160/96	170/110	5 10
11	168/112 150/100 170/120	132/90 140/98 140/98	150/100	7 13
12	205/130 150/96	170/120 140/100	180/125	6
13	200/135 158/118	150/110 144/100	160/120	11
14	160/110 140/90	140/90 140/90	150/96	11
15	185/125 168/110	150/110 144/100	160/110	9
16	180/125 140/110 164/90	145/104 126/80 140/80	155/110	5 9
17	225/145 118/88 162/98	160/100 110/86 156/96	190/120	6 10
18	160/110 118/?	136/88 110/?	148/100	8
19	200/120 176/108	152/100 160/108	176/110	8
20	224/118 180/90	150/88 170/90	190/110	8
21	196/146 164/102	160/96 160/100	180/130	8
22	212/150 168/110	160/100 128/94	175/120	6
23	208/122 155/110	130/95		6
24	195/125 184/108	145/90 150/96	160/100	4
25	180/150 145/110	130/95 136/102	150/120	5
26	230/150 112/78	188/108 112/70		5
27	204/124 142/90	130/50 138/88		4
28	220/140 168/102	120/75 150/100		4
29	230/156 175/125	170/110 115/88	190/130	3

results from operation than did men (table 8). Known duration of hypertension did not significantly influence the effects of operation on blood pressure (table 9). Age did not greatly influence the percentage of good

TABLE VIII

Influence of Sex of Patients on Effect of Operation on Blood Pressure

Result of operation	Sex	
	Men	Women
Failure or temporary	27*	31
Fair	14	21
Good	11	17

* Number of patients.

Women: Good or fair results = 55%
Men: Good or fair results = 48%

TABLE IX

Influence of Known Duration of Hypertension on Effect of Operation on Blood Pressure

Results of operation	Duration, years			
	2 or less	3–4	5–6	7 or more
Failure or temporary	22*	18	10	8
Fair	10	11	4	8
Good	9	8	4	5

* Number of patients.

2 years or less, good or fair results = 46%
3 to 4 years, good or fair results = 51%
5 to 6 years, good or fair results = 44%
7 years or more, good or fair results = 62%

or fair effects of operation on blood pressure although patients in the third decade of life received a slightly smaller percentage of good or fair results than did those in the fourth, fifth, and sixth decades of life (table 10).

TABLE X

Influence of Age of Patients on Effect of Operation on Blood Pressure

Results of operation	Age in decades			
	Third	Fourth	Fifth	Sixth
Failure or temporary	10*	17	20	7
Fair	2	14	12	3
Good	4	12	7	4

* Number of patients.

(1) Third decade, good or fair results = 37%
(2) Fourth decade, good or fair results = 60%
(3) Fifth decade, good or fair results = 50%
(4) Sixth decade, good or fair results = 50%

The group of the hypertension * did not greatly influence the results of operation on the blood pressure although there was a slightly smaller percentage of good or fair results among patients who had hypertension group 3 than among those who had hypertension group 2 (table 11). One patient

TABLE XI

Influence of Group of Hypertension on Effect of Operation on Blood Pressure

Results of operation	Group of hypertension		
	2	3	4
Failure or temporary	31*	28	1
Fair	19	15	
Good	18	10	

* Number of patients.

Group 2; good or fair results = 54%
Group 3; good or fair results = 47%

operated on, who had hypertension group 4, did not receive any benefit from operation (table 11). The degree of sclerosis of the retinal arteries influenced greatly the result of operation on the blood pressure (table 12).

TABLE XII

Influence of Degree of Sclerosis of Retinal Arteries on Effect of Operation on Blood Pressure

Results of operation	Degree of sclerosis of retinal arteries			
	None	1	2	3
Poor	1*	13	33	14
Fair	2	4	25	2
Good	3	10	13	2

* Number of patients.

No sclerosis; good or fair results = 83%
Sclerosis 1; good or fair results = 52%
Sclerosis 2; good or fair results = 53%
Sclerosis 3; good or fair results = 22%

Those who had no detectable sclerosis of the retinal arteries received good or fair results in 83 per cent of instances, while those who had sclerosis of the retinal arteries, graded 1 or 2, received good or fair results in 50 per cent of instances, and those who had sclerosis graded 3 of the retinal arteries received good or fair results in only 22 per cent of instances. These results indicate definitely that patients who have advanced organic arterial disease resulting from hypertension are less benefited by operation than are patients who have little or no demonstrable organic arterial disease.

We have attempted to predict the effect of operation on blood pressure by a study of the response of the blood pressure to rest, administration of 3

* The division of the hypertension into groups has been described previously.[5]

grains (0.2 gm.) of sodium amytal hourly for three successive doses, and the slow intravenous injection of a 5 per cent solution of pentothal sodium. In a previous communication we stated, "It is well to emphasize again that errors in prediction of effects of operation on blood pressure are rarely made when preoperative tests indicate a poor result but that errors of prediction occur occasionally when preoperative tests indicate a good result of operation. As a result of these observations we feel justified ordinarily in refusing to operate on patients when preoperative tests indicate that response of the blood pressure to operation will be unsatisfactory." [5] The present study emphasizes that it is easier to be accurate in prediction of poor results of operation on blood pressure than it is to be accurate in prediction of good results.[4] Thus, when the diastolic blood pressure decreased to less than 110 as a result of the intravenous injection of pentothal sodium,[6] good results occurred seven times as frequently as when the diastolic pressure did not decrease to less than 110. When the diastolic pressure decreased to less than 110 as a result of the oral administration of 9 grains (0.6 gm.) of sodium amytal divided in three hourly doses, good or fair results occurred almost four times as frequently as when the diastolic blood pressure decreased to a figure greater than 120. When the diastolic blood pressure decreased to less than 100 as a result of rest, good or fair results occurred three times as frequently as when it did not decrease to less than 120 mm. of mercury. When the maximal diastolic blood pressure observed was less than 130, good results of operation occurred three times as frequently as when the maximal diastolic blood pressure observed exceeded 150 mm. of mercury. Unfortunately for accuracy of preoperative prediction, there were many instances of eventual poor effects of operation on blood pressure in which the response of the diastolic blood pressure to the measures mentioned was entirely adequate. These studies emphasize that there are no criteria by which it is possible to select patients for operation with certainty. However, there are trends.

It is possible to outline the circumstances under which the probabilities are good that the patient will get a good result from operation. This is true when the diastolic blood pressure decreases to less than 110 as a result of rest, administration of amytal and injection of pentothal and when sclerosis of the retinal arteries is absent or slight. It is possible, also, to outline a situation in which the probabilities are small that a patient will receive good results from operation. Such a situation is present when there is advanced sclerosis of the retinal arteries, when the maximal diastolic blood pressure exceeds 150, when the diastolic pressure does not decrease to less than 120 as a result of rest, intravenous injection of pentothal sodium or administration of sodium amytal. In the field between those represented by these two groups of patients is a large number of patients for whom no accurate prediction can be made as to whether they will receive significant effect on blood pressure as a result of operation.

Now that it has been demonstrated that the operation can be carried out safely, that it does not disable and that it frequently produces remarkable effects on blood pressure, we believe that operation should be performed on patients whose hypertension is mild, particularly if blood pressure is progressively elevated. In the past it has been our policy to wait to see if the blood pressure is elevated progressively in instances in which elevation of blood pressure is not great. Now, however, we believe that many patients who have mild hypertension should be operated on, particularly if there are peaks of great elevation of blood pressure, a situation which can be assumed when there is great increase of the blood pressure as a result of immersion of a hand in ice water.[12] While it is true that the hypertension of an occasional patient remains mild, in most instances the blood pressure is progressively elevated and if operation is deferred, it may be deferred too long. In considering operation for patients with mild hypertension it is well to consider the consequences of hypertension which usually occur several years later. It is to prevent these consequences that some remedy is desperately needed and while extensive sympathectomy may not be the ideal remedy there is much evidence that it may prevent or delay the complications of hypertension which all too frequently cause death in the most productive periods of patients' lives. It seems apparent that little can be accomplished when the hypertension is severe, when it does not respond satisfactorily to rest, administration of sodium amytal and pentothal sodium and when there is advanced sclerosis of the retinal arteries. It is useless to operate on patients who have any significant renal insufficiency, congestive heart failure, angina pectoris or a cerebral vascular accident from which recovery has not been satisfactory.

Conclusions

1. Extensive sympathectomy can be carried out safely for patients with essential hypertension. The operation does not disable and it produces only minor effects on sexual function, sweating and the intestines.

2. Headache, nervousness, and pain in the left side of the thorax are relieved in a high percentage of instances, regardless of whether the effects of operation on the blood pressure are poor or good. Dyspnea and fatigue with exertion occur commonly after operation but tend to disappear gradually.

3. The effects of operation on the blood pressure are not constant. They vary from poor to good. No infallible method of selecting patients for operation is available. However, a situation exists in which the probabilities of good effects on the blood pressure are great and another situation exists in which the probabilities of good effects of operation on the blood pressure are small.

4. As a result of our experience with extensive sympathectomy for essential hypertension, we believe that it is advisable to operate on more patients

who have mild hypertension and on fewer patients who have severe hypertension.

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GASTRIC LESIONS ASSOCIATED WITH PERNICIOUS ANEMIA *

By RICHARD N. WASHBURN, M.D., and HENDRIK M. ROZENDAAL, M.D.,†
Rochester, Minnesota

THE occurrence of gastric lesions in association with pernicious anemia has frequently been discussed in the medical literature and the development of gastric carcinoma in the course of the disease has been described. The fact that carcinoma has been observed is not surprising in view of the development of pernicious anemia at an age when malignant disease is common. However, a review of reported cases seems to indicate that the incidence of gastric carcinoma in association with pernicious anemia is higher than would be expected on the basis of coincidence. If the factors involved in the genesis of pernicious anemia predispose to the development of malignant change in gastric mucosa, a gradual increase in the number of cases in which gastric carcinoma is associated with pernicious anemia would be expected as a result of the more adequate treatment of pernicious anemia and its favorable effect on life expectancy.

Giffin and Bowler reviewed a series of 628 cases of pernicious anemia which were observed at The Mayo Clinic between January 1917, and January 1922. In this group of cases one patient had been found to have a gastric carcinoma 18 months after definite indications of pernicious anemia had been recognized.

Conner and Birkeland reported a review of 658 cases of pernicious anemia observed at The Mayo Clinic from 1928 to 1930. In four, or 0.6 per cent, of these cases there also was a carcinoma of the stomach. They reported seven additional cases, not in the foregoing group, in which cöexistence of these conditions was certain or almost certain. In this group of 11 cases, pernicious anemia had preceded the onset of carcinoma in two cases; in two cases, the carcinoma was found before a diagnosis of pernicious anemia was made, and in seven cases there was an almost simultaneous occurrence.

Priestley and Heck reported three cases of pernicious anemia in which malignant polypoid gastric lesions were present. In one case the symptoms of pernicious anemia had preceded the onset of the gastric symptoms by at least three years. In one case the gastric symptoms and the anemia apparently had developed simultaneously, and in the third case no subjective gastric symptoms were present.

We have reviewed 906 cases in which a definite diagnosis of pernicious anemia was made. The patients in these cases were seen at the clinic between 1931 and 1934. In approximately 60 per cent of the cases a roent-

* Submitted for publication May 10, 1937.
† Now residing in Schenectady, New York.

genologic study of the stomach was made, and gastric lesions were found in 24 cases; eight of these lesions were benign. Therefore, in this group of 906 cases of pernicious anemia, gastric carcinoma was found in 16 cases, or 1.76 per cent. Of these 16 cases two have previously been reported by Priestley and Heck and three have been reported by Conner and Birkeland; 11 cases will be reported briefly in this paper.

Cases in Which Pernicious Anemia Was Present Prior to the Onset of Gastric Symptoms

Case 1. A farmer, aged 66 years, was admitted to the clinic on October 26, 1931. For a year and a half before he came to the clinic, he had been taking liver extract for anemia. Examination revealed a markedly atrophic tongue and a moderate degree of anemia. Hematologic studies showed 9.6 gm. of hemoglobin per 100 c.c. of blood, 2,360,000 erythrocytes and 4,000 leukocytes per cubic millimeter of blood, marked anisocytosis and slight polychromatophilia. Achlorhydria was present. Roentgenologic examination of the stomach did not disclose any abnormality. The patient was given an adequate amount of liver extract and made an excellent response. Examination in 1932 revealed that he was in very good health. He returned to the clinic in October 1934, after he had neglected the prescribed treatment. The value for the hemoglobin was 10.7 gm. per 100 c.c. of blood; there were 2,720,000 erythrocytes and 6,700 leukocytes in each cubic millimeter of blood and the morphologic blood picture was that of pernicious anemia. Roentgenologic examination of the stomach again failed to disclose any abnormality. Prompt recovery followed intensive treatment with liver extract.

In January 1935, the patient began to complain of gaseous indigestion, and a gradual loss of weight was noted during the next four months. When he was examined at the clinic on May 17, 1935, the value for the hemoglobin was 15.9 gm. per 100 c.c. of blood, there were 4,690,000 erythrocytes and 8,400 leukocytes per cubic millimeter of blood and the morphologic blood picture was normal. Physical examination revealed a movable firm mass in the epigastrium and enlargement of the liver. Roentgenologic examination disclosed a scirrhous carcinoma which involved the upper two-thirds of the stomach. Exploratory laparotomy was performed by Dr. Walters on May 24, 1935. He found inoperable carcinoma of the stomach and many metastatic nodules in the liver. A biopsy was not performed.

Comment. This patient had pernicious anemia for at least five years before symptoms of gastric carcinoma developed, and roentgenologic examination of the stomach on two occasions did not reveal any abnormality.

Case 2. A farmer, 64 years old, came to The Mayo Clinic on July 25, 1932, complaining of weakness and anemia. These symptoms had been present since 1930, when examination had revealed the presence of achlorhydria and anemia. Roentgenologic examination of the stomach at that time had not disclosed any abnormality. The patient had taken liver extract orally and promptly had regained strength and color. He had enjoyed good health from 1930 to 1932, except when treatment had been neglected. Three weeks before he came to the clinic he had had a recurrence of weakness and pallor. He had been hospitalized and roentgenograms of the stomach had revealed a tumor.

Examination at the clinic revealed a thin, pale, elderly, white man. The value for the hemoglobin was 12 gm. per 100 c.c. of blood; there were 3,280,000 erythrocytes and 10,400 leukocytes in each cubic millimeter of blood and the morphologic

features of the blood were typical of pernicious anemia. Gastric analysis revealed achlorhydria and the presence of fresh blood. Roentgenologic examination of the stomach showed an extensive, ulcerating, polypoid lesion. The patient was hospitalized and liver extract was administered parenterally. On August 8, 1932 subtotal gastrectomy was performed; a Billroth II type of anastomosis was established. Examination of the resected portion of the stomach revealed an ulcerating, polypoid carcinoma, grade 3. There was involvement of the regional lymph nodes. The patient returned to his home and died on February 19, 1933. Necropsy was not performed.

Comment. In this case the symptoms of pernicious anemia were present at least two years before gastric carcinoma was discovered.

Case 3. A physician, aged 65 years, was first seen at the clinic on November 2, 1932. In 1925 he had started to take liver because of anemia and the response had been good. In 1928 he first had noticed numbness and tingling of the fingers and toes and difficulty in walking. These symptoms had improved following an increase in the dose of liver. Six months before he came to the clinic, nausea, anorexia, malaise, and an occasional cramping sensation in the abdomen had developed. Slight relief had been obtained by drinking warm milk. Physical examination revealed a movable mass in the epigastrium which extended upward under the left costal margin. The value for the hemoglobin was 13.7 gm. per 100 c.c. of blood and there were 3,890,000 erythrocytes and 4,900 leukocytes in each cubic millimeter of blood. Examination of blood smears revealed the features of pernicious anemia. Gastric analysis showed achlorhydria. A roentgenogram of the stomach showed extensive scirrhous carcinoma. Exploration of the stomach was advised but refused. The patient died shortly after his return home.

Comment. The typical findings of pernicious anemia were present seven years before there were any gastric symptoms. The gastric symptoms were rather mild but the patient had a very extensive carcinoma.

Case 4. A married woman, aged 60 years, came to the clinic June 25, 1928. In the preceding year she had suffered from weakness, loss of weight, and anemia. At times she had noticed slight soreness of the tongue and numbness and tingling of the fingers. Physical examination revealed only a smooth tongue. The value for the hemoglobin was 45 per cent (Dare) and there were 2,530,000 erythrocytes and 4,900 leukocytes in each cubic millimeter of blood. Examination of blood smears showed slight poikilocytosis and anisocytosis, which were suggestive of pernicious anemia. Gastric analysis revealed achlorhydria. A roentgenogram of the stomach did not disclose any abnormality. Raw liver was given by mouth and immediate improvement was noted. The patient returned to the clinic on April 28, 1931. Except for slight numbness and tingling of the fingers, she had done well on liver treatment. The value for the hemoglobin was 15.4 gm. per 100 c.c. of blood and there were 3,860,000 erythrocytes and 6,700 leukocytes in each cubic millimeter of blood. Definite macrocytosis, poikilocytosis, and anisocytosis were present. When the patient again returned to the clinic, on June 22, 1932, she felt well and did not have any symptoms which were referable to the gastrointestinal tract. However, on November 8, 1932, she reported that she had marked indigestion during the past three months and slight soreness in the epigastrium which had been worse after meals and relieved by vomiting. She had lost much weight. Physical examination revealed a questionable mass in the epigastrium. The value for the hemoglobin was 16.4 gm. per 100 c.c. of blood; there were 3,850,000 erythrocytes and 9,600 leukocytes in each cubic millimeter of blood. Examination of blood smears showed slight macrocytosis.

Roentgenologic examination of the stomach disclosed polyposis of the distal half. Dr. Walters, who performed an abdominal exploration on November 14, 1932, found an inoperable carcinoma of the stomach and a metastatic mass in the pelvis. Specimens of the omental lymph nodes revealed adenocarcinoma, grade 4. The patient died six weeks following the operation; necropsy was not performed.

Comment. In this case pernicious anemia preceded the roentgen demonstration of carcinoma of the stomach by at least four years. The condition of the patient was carefully followed in the interim and the blood picture and blood count returned to normal under treatment, in spite of the presence of extensive carcinoma of the stomach.

Case 5. A physician, aged 63 years, entered the clinic on September 25, 1931. A year and a half previously, numbness and tingling of the fingers and toes had developed; at that time the value for the hemoglobin had been 40 per cent and the erythrocytes had numbered 1,300,000 per cubic millimeter of blood. Achlorhydria had been found. Following the use of liver, the patient had noted marked improvement. He had felt fairly well until six months before he came to the clinic, at which time he had begun to experience distress in the epigastrium. This had come on about two hours after meals. He had lost 10 pounds (4.5 kg.) in three months. Physical examination disclosed a palpable mass in the epigastrium. The value for the hemoglobin was 13.7 gm. per 100 c.c. of blood; there were 4,320,000 erythrocytes and 6,300 leukocytes in each cubic millimeter of blood. The morphologic picture was not diagnostic of pernicious anemia. Roentgenologic examination of the stomach showed an ulcerating carcinoma. Abdominal exploration, which was performed by Dr. Judd, on October 21, 1931, revealed carcinoma of the lesser curvature of the stomach and metastatic nodules in the liver. No specimens were taken for biopsy. The patient was treated with radium at home, but became weaker and died January 26, 1932.

Comment. The onset of symptoms of pernicious anemia antedated that of the gastric lesion by at least one year. Gastric symptoms developed rapidly after the onset; however, the blood count was almost normal when the patient came to the clinic, six months later.

Case 6. A farmer, aged 50 years, registered at the clinic May 18, 1927. For two years he had complained of loss of weight and weakness, and had become pale. For a month before he came to the clinic he had noticed numbness and tingling of the fingers and toes. Physical examination revealed evidence of marked anemia. The value for hemoglobin was 30 per cent (Dare); the erythrocytes numbered 1,280,000 and the leukocytes numbered 5,100 per cubic millimeter of blood. Examination of blood smears showed anisocytosis and poikilocytosis. Achlorhydria was present. Roentgenologic examination of the stomach did not disclose any abnormality. A high vitamin diet and later on the use of liver and dilute hydrochloric acid were prescribed. Marked improvement followed. When the patient returned to the clinic October 30, 1934, he said that he had been well until six months previously, when severe burning pain had occurred in the epigastrium about two hours after each meal. Moderate relief had been obtained by drinking milk. He had been treated for ulcer of the stomach. He had lost 25 pounds (11.3 kg.) during the preceding six months. One year preceding the patient's last visit to the clinic a small lesion had developed on the lower lip and had been growing slowly. Examination revealed that this lesion was an epithelioma which was 4 cm. in diameter; biopsy disclosed a squamous cell carcinoma, grade 3. An indefinitely outlined, firm, tender

mass was present in the epigastrium. The value for the hemoglobin was 7.9 gm. per 100 c.c. of blood; there were 3,730,000 erythrocytes and 8,800 leukocytes in each cubic millimeter of blood. The blood smears were not diagnostic of pernicious anemia. Roentgenologic examination of the stomach revealed an extensive polypoid carcinoma which involved the greater portion of the organ. Operation was not advised. Radium was applied to the lesion on the lip. The patient returned home and died on February 23, 1935.

Comment. In this case an interval of more than eight years elapsed between the onset of symptoms referable to pernicious anemia and those of gastric carcinoma. A malignant lesion of the lip developed before the onset of gastric symptoms.

Case 7. A farmer, 59 years of age, was first seen at the clinic in January 1921. He had noticed increasing weakness, dyspnea, and numbness of fingers and toes 18 months prior to his admission to the clinic. Examination revealed an atrophic tongue, marked anemia, and evidence of subacute combined sclerosis. The value for the hemoglobin was 25 per cent and there were 1,140,000 erythrocytes in each cubic millimeter of blood. Marked anisocytosis and poikilocytosis were present. Achlorhydria was found. Many blood transfusions were given and the patient made a fair recovery.

When he returned to the clinic in July 1935, he complained of poor appetite and gradual weight loss in spite of administration of ventriculin. The value for the hemoglobin was 9.15 gm. per 100 c.c. of blood; there were 1,980,000 erythrocytes in each cubic millimeter of blood. The morphologic picture of the blood was that of pernicious anemia. Roentgenologic examination of the stomach showed an extensive, inoperable carcinoma which involved the entire cardia; there was no evidence of obstruction. The patient made satisfactory improvement following administration of liver extract, and returned to the clinic in December 1936. He had lost 25 pounds (11.3 kg.) in three months. There was no definite anemia but the morphologic study of the blood still showed characteristics of pernicious anemia. Roentgenologic examination revealed that the gastric lesion had increased definitely in size but no evidence of obstruction was present.

Comment. The patient had typical symptoms and findings of pernicious anemia at least 15 years prior to the discovery of an extensive carcinoma of the stomach. The anemia remained easily controllable in spite of the progression of the gastric lesion.

Cases in Which the Development of Gastric Carcinoma and Pernicious Anemia Apparently Was Simultaneous

Case 8. A laborer, aged 53 years, was admitted to the clinic January 29, 1934. He had been in good health until two months before, when he had begun to lose weight and strength; at the same time, he had noticed numbness in the fingers. The results of physical examination were essentially negative. The value for the hemoglobin was 10.35 gm. per 100 c.c. of blood; there were 2,450,000 erythrocytes and 8,300 leukocytes in each cubic millimeter of blood. Examination of blood smears revealed slight poikilocytosis, polychromatophilia, and marked anisocytosis. Achlorhydria was found. Roentgenologic examination of the stomach disclosed a polypoid carcinoma of the greater curvature. Following intramuscular injections of liver extract, marked reticulocytosis was noted. Exploratory laparotomy, which was performed by Dr. Judd, on February 12, 1934, revealed a large carcinoma which in-

volved practically the entire wall of the stomach. Resection was impossible. Biopsy disclosed a papillary adenocarcinoma, grade 2. The patient died on August 11, 1934. No necropsy was performed.

Comment. In this case the development of the gastric symptoms was concurrent with that of the symptoms of pernicious anemia.

Case 9. A physician, aged 53 years, was admitted to the clinic September 28, 1931. For two years he had complained of mild soreness of the tongue; anemia and numbness and tingling in the hands and feet had developed gradually. The results of physical examination were essentially negative. Neurologic examination revealed evidence of subacute combined sclerosis. The value for the hemoglobin was 11.5 gm. per 100 c.c. of blood; the erythrocytes numbered 3,890,000 and the leukocytes numbered 12,700 per cubic millimeter of blood. Morphologic examination of blood smears showed the typical features of pernicious anemia with moderate anisocytosis and slight polychromatophilia. Achlorhydria was found. Roentgenologic examination of the stomach revealed an extensive polyposis of the distal half. Following intramuscular injections of liver extract, a marked rise in the percentage of reticulated erythrocytes was noted. On October 3, 1931, Dr. Balfour performed partial gastrectomy followed by a Billroth I anastomosis. The pathologic report read: multiple polypi, largest 2 cm. in diameter; carcinoma, grade 1. On inquiry in August 1934, the patient reported that he was in good general health with the exception of slight increase in the intensity of the neurologic symptoms.

Comment. A case of multiple, malignant gastric polypi is described in which the symptoms developed concurrently with those of pernicious anemia.

Case 10. A married woman, aged 40 years, was admitted to the clinic on April 28, 1920. She had a small adenomatous goiter but there was not any evidence of hyperthyroidism. The value for the hemoglobin was 69 per cent; there were 3,780,000 erythrocytes and 5,800 leukocytes in each cubic millimeter of blood. She was given iron for treatment of secondary anemia. The patient returned to the clinic January 12, 1928. Eight months previously she had begun to complain of indefinite epigastric distress, weakness, and pallor. Occasional soreness of the tongue and numbness of the hands and feet were noted. Two months later it was found that achlorhydria was present. The patient was given a liver diet; she gained in weight and strength. Physical examination at the clinic in January 1928, revealed an irregular mass in the left hypochondrium. The value for the hemoglobin was 48 per cent (Dare); there were 3,210,000 erythrocytes and 9,800 leukocytes in each cubic millimeter of blood. Roentgenologic examination of the stomach disclosed a carcinoma which extended high on the lesser curvature. On January 25, 1928, Dr. Judd removed four-fifths of the stomach because of extensive carcinoma. The pathologist reported that the tumor was a small-cell carcinoma. When the patient returned to the clinic May 21, 1928 she still complained of soreness of the tongue and tingling of the feet. The value for the hemoglobin was 40 per cent; there were 3,940,000 erythrocytes and 5,500 leukocytes in each cubic millimeter of blood. Moderate anisocytosis, poikilocytosis, and polychromatophilia were present. She was given iron and dilute hydrochloric acid. In June 1929, the value for the hemoglobin was 73 per cent and there were 4,470,000 erythrocytes and 6,300 leukocytes in each cubic millimeter of blood. Slight anisocytosis and poikilocytosis also were present. In 1932, marked anemia developed. Definite macrocytosis was present. She made rapid improvement following the administration of liver.

Comment. A definite diagnosis of pernicious anemia was not made at the time the carcinoma of the stomach was discovered. However, in view

of the history it is very likely that symptoms of pernicious anemia were present at that time. Following resection of a large portion of the stomach, hypochromic anemia developed. This responded to the administration of iron. At a later time the blood picture became characteristic of pernicious anemia and a prompt response to liver treatment followed.

Case 11. A lawyer, aged 60 years, was admitted to the clinic on August 11, 1933. Seven years before he came to the clinic diabetes had been discovered. For a year before his registration at the clinic he had complained of weakness and pallor. Eight months before his admission the value for the hemoglobin had been 29 per cent (Dare) and the number of erythrocytes in each cubic millimeter of blood had been 1,400,000. A diagnosis of pernicious anemia had been made and treatment with liver had been instituted. Prompt recovery had followed. Roentgenologic examination of the stomach had not disclosed any abnormality. During the year before he came to the clinic pain had developed in the upper part of the abdomen. This pain had not been definitely related to meals. The results of physical examination at the clinic were essentially negative. The value for the hemoglobin was 13.3 gm. per 100 c.c. of blood; there were 4,150,000 erythrocytes and 7,700 leukocytes in each cubic millimeter of blood. Slight macrocytosis and a right shift of the neutrophiles were observed. Achlorhydria was present. Roentgenologic examination of the stomach revealed a carcinoma which involved the middle third. On August 18, 1933, Dr. Gray performed a sleeve resection of the middle third of the stomach. The pathologist reported that the tumor was an ulcerated adenocarcinoma, grade 3, which had involved the lymph nodes. Ventriculin was prescribed and the patient was dismissed September 4, 1933. He returned to the clinic on February 8, 1935 because of symptoms of recurrence of the carcinoma and gastric obstruction. Jejunostomy was performed. The blood count was normal. The patient died June 24, 1935.

Comment. In this case the onset of pernicious anemia and that of carcinoma of the stomach were apparently concurrent.

Cases in Which Pernicious Anemia Was Associated with Gastric Polyps

In the remaining eight cases of this report, gastric polyps were demonstrated either by roentgenologic examination (six cases) or by operation (two cases). The frequency with which polypoid lesions of the stomach were found is striking. This corresponds with the observation of M. R. Brown, who reported the postmortem findings in 151 cases of pernicious anemia; she found benign tumors of the gastrointestinal tract. In ten of these cases one or more polyps were found in the stomach. In one case carcinoma of the stomach was present.

Recently, Faber has emphasized the occurrence of gastritis, with or without severe atrophy of the mucous membrane, in cases of pernicious anemia. He expressed the opinion that polyposis of the stomach always develops on the basis of a preëxisting gastritis. According to Hurst and Konjetzny, the presence of chronic atrophic gastritis is the predisposing factor for the development of both gastric polyps and gastric carcinoma.

Wilkinson in 1933 studied the incidence of malignant disease in a group of 370 cases of pernicious anemia and found it to be present in six cases; in

only one of the cases was the malignant growth in the stomach. He reviewed the literature and found 35 cases in which both primary anemia and malignant disease were present. In 26 of these cases there was carcinoma of the stomach and in the remaining nine cases the neoplasm was found elsewhere. In 24 of the cases the diagnosis of pernicious anemia had been made before the presence of carcinoma was discovered. In only two instances was the malignant growth identified first. He was not convinced that there was a relationship between the development of the two diseases.

Strandell in 1931 reported four instances of gastric carcinoma in 117 cases of pernicious anemia. In two of these cases a diagnosis of pernicious anemia had been made several years prior to the onset of gastric symptoms. In a group of 440 cases of pernicious anemia recently reported (1936) by Murphy and Howard, carcinoma of the stomach was found in four cases and in three of these cases the gastric lesion was discovered several years following the first symptoms of the anemia. Hurst has observed five cases in which pernicious anemia was associated with gastric malignant neoplasm. Miller reported two cases in which gastric carcinoma developed in the course of pernicious anemia. In another case the onset of symptoms of gastric carcinoma and the onset of the symptoms of pernicious anemia were simultaneous. In 115 cases of pernicious anemia Groen observed two cases in which carcinoma was present and in both instances the carcinoma developed many years after the onset of the anemia. Silverman, Grill, Weil and Bernard, Plummer and Simpson, and Van der Sane each have reported one case in which pernicious anemia had been present several years before a gastric carcinoma was found. Brandes reported the results of necropsy in 27 cases of pernicious anemia and found gastric carcinoma in four instances.

Summary

A series of 906 consecutive cases of pernicious anemia has been reviewed. Gross gastric lesions were found in 24 cases. In 16 cases, gastric carcinoma was found, an incidence of 1.76 per cent. Eleven of these 16 cases have been reported in this paper; the remaining five cases have been reviewed previously. In seven of the 11 cases the gastric lesion developed some time after the diagnosis of pernicious anemia had been made, and in four instances the two diseases apparently developed concurrently. In eight other cases, benign polypoid lesions were found.

From the literature, including the cases just reported, we were able to collect 75 cases in which pernicious anemia and gastric carcinoma coexisted. In 49 of these cases the gastric carcinoma developed during the course of the pernicious anemia.

From a comparison of the study of this material with a similar study made by Giffin and Bowler and by Conner and Birkeland, it appears that there is some evidence of an increasing frequency of gastric lesions in the course of pernicious anemia.

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TUBERCULOSIS IN MEDICAL AND NURSING HOSPITAL PERSONNEL *

By J. Arthur Myers, F.A.C.P., Benedict Trach, Harold S. Diehl and Ruth E. Boynton, *Minneapolis, Minnesota*

In a previous paper [1] reports were presented on three private hospital schools of nursing in which the students were observed with reference to tuberculosis. The hospital of School I operated a tuberculosis division where every student nurse at some time before graduation was compelled to spend three months. In the hospitals of Schools II and III there was no special division but occasional tuberculous patients were admitted for both diagnosis and treatment. These observations have been continued and have brought about so much enlightenment among the personnel that some of our hospitals are now taking steps to control the disease which they would not even have considered in 1929 when our work began. Moreover, as a result of these studies, other hospitals of the same community have adopted worth while tuberculosis programs for their students of nursing.

The tuberculin test of the student on her admission to a school of nursing has brought to light important facts not only with reference to the individual but also to the number in this age group whose bodies contain primary tuberculosis complexes. The positive tuberculin reaction establishes a diagnosis of the primary complex regardless of the presence or absence of shadows on the roentgen-ray film, just as the Wassermann, Kahn or Kline tests are usually diagnostic of syphilis even in the absence of demonstrable lesions.

The annual testing of entering students in schools of nursing has shown a decrease in the incidence of positive reactors among girls of this age period. For example, in figure 1, School I, the incidence of positive reactors on admission was 39.29 per cent in 1929, whereas it was only 4.25 per cent in the entering class of 1935. In School II in the fall of 1929, the incidence of positive reactors was 27.78 per cent, while in 1935 it was only 3.57 per cent. In these two schools the incidence for 1935 was the lowest of any year during our period of observation. In School III the incidence of positive reactors in the entering class of 1929 was 27.03 per cent, while in 1935 it was 24 per cent. In this school, some classes have shown a good

* Presented in part before the joint meeting of the Philadelphia Medical Society and the Pennsylvania Tuberculosis Association, January 20; the Colorado Tuberculosis Association and the Denver Sanatorium Association, Denver, February 22; the Academy of Medicine, Toledo, Ohio, May 21; the 32nd annual meeting of the American Sanatorium Association, Milwaukee, Wisconsin, May 31; and the joint meeting of the Medical Society of the County of Queens and the Queensboro Tuberculosis and Health Association, Jamaica, New York, September 22, 1937.

Prepared with the aid of a grant from the Medical Research Fund, University of Minnesota.

From the Departments of Preventive Medicine and Internal Medicine, University of Minnesota, and the Lymanhurst Health Center, Minneapolis, Minn.

deal lower percentage of positive reactors on admission. Thus, the number of girls entering our schools of nursing with potential remote hazards from tuberculosis is becoming small.

From the beginning we strongly recommended roentgen-ray film examinations of the chests of all of the entering students who reacted positively to the tuberculin test and this to be followed by careful clinical and laboratory examinations of all who presented parenchymal shadows on the roentgen-ray film, in order to determine whether the shadows were due to tuberculosis or some other condition, and if to tuberculosis as to whether the disease was progressive.

One must be extremely cautious on the entrance examinations not to make diagnoses of etiology from shadows on roentgen-ray films even among positive tuberculin reactors. We have seen injustice done girls whose

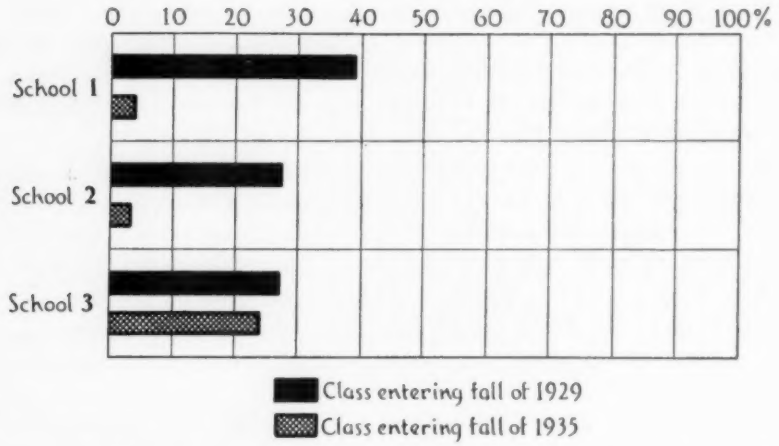

FIG. 1. Per cent of positive tuberculin reactors in two entering classes of student nurses.

shadows proved to be due to unresolved pneumonia but the interpreters of the films not knowing of the recent existence of pneumonia made frank diagnoses of tuberculosis which barred the students from the schools before the clinicians had an opportunity to examine them.

Occasionally, on entrance examinations among the positive tuberculin reactors, one finds the girl who already has demonstrable chronic pulmonary tuberculosis which is in the presymptom stage. To find such an area of disease is of great value to the individual student, since it can usually be treated so successfully that she will neither fall ill from that particular lesion nor will she spread tubercle bacilli to her associates. The finding of such a lesion is also of great value to the school of nursing, the hospital in which she works, and to all of her associates outside the hospital, since if the lesion is not detected it is likely to progress to extensive proportions before it produces symptoms and often tubercle bacilli are being eliminated in large numbers before the disease is detected.

In School III, it was impossible, at first, to convince the authorities of the value of the roentgen-ray film of positive tuberculin reactors. These girls appeared so healthy that it seemed unbelievable that their lungs might contain lesions which would ultimately convert them into textbook picture consumptives. However, in 1934, a second year student nurse who had reacted positively to the test on admission but appeared well had a pulmonary hemorrhage while at work. The examination revealed evidence of cavity formation in one lung and tubercle bacilli were abundantly present in the sputum. In communicating with her family physician in another city, we were able to obtain films of her chest which were made two or three years before she entered the school of nursing. These films revealed definite shadows which clinical examination had then proved to be due to tuberculosis. Thus, because of failure to make films of the chests and the necessary subsequent examinations of positive tuberculin reactors on admission, this girl was permitted to spread bacilli among the students, the patients, and her other associates. However, this case convinced the authorities that routine roentgen-ray films of the chests of positive tuberculin reactors are valuable and since that time a good tuberculosis control program has been in effect in this school.

Indeed, in each of these three schools we have finally been able to develop a program for examining student nurses which we believe closely approaches the ideal. It consists of administering the tuberculin test to every probationer as soon as possible after entering the school. All of the positive reactors immediately have roentgen-ray films of their chests. If there is no abnormal finding on the roentgen-ray film or even if there is evidence of the existence of the primary complex in the lung or hilum, each student has a roentgen-ray film examination annually as long as she remains in the school. All who react negatively to tuberculin have the test repeated every six months as long as they remain negative. Those who at any time change from negative to positive immediately have roentgen-ray films of the chests and annually thereafter. During their course in training, we attempt to convince the positive reactors that they should never let a year pass without having roentgen-ray film examinations of the chest and to convince the negative reactors on graduation that at least annually they should have the tuberculin test repeated and if at any time they become positive reactors, they should have films made of the chest at least once every year.

An attempt is made to have the girls understand the significance of the tuberculin test before they graduate. They are told that a positive reaction indicates at least one and probably several primary tuberculosis complexes in their bodies, that in the foci of these complexes, bacilli may remain alive and virulent for years, even for the remainder of their lives; that at any time, the bacilli may escape and set up clinical disease. The attention of the students is called to the statement of Wallgren,[2] as follows: ". . . indirectly,

primary tuberculosis is the starting-point also for tuberculous diseases of a quite different nature, such as meningitis, pleurisy, miliary tuberculosis and last, but not least, tertiary pulmonary tuberculosis." A similar expression by Smith [3] is significant: "As a matter of fact, there can be no infection without disease since infection with the tubercle bacillus means that it has lived and grown in the body of its host and has set up its characteristic pathological lesions. No matter how small, how deeply seated, how obscure such lesions may be, they always carry the threat of serious results from dissemination."

In order to stimulate interest among the nurses, themselves, as well as to protect them and the public they later serve, School III has arranged for a provision whereby the Commissioner of Health issues a certificate to every girl on graduation whose examination has revealed her to be free from clinical tuberculosis in communicable form and who has been immunized against such diseases as smallpox and diphtheria. The girls who receive such certificates are advised to have them renewed annually on the basis of adequate examination.

Failure on the part of a school of nursing to examine its students and protect them against tuberculosis may later result in disaster, not only for the nurse, herself, but for her patients. A good example is that of a graduate nurse whose training school did not examine its students adequately during their student days or at the time of graduation. This girl was employed by a general hospital in a small city. Unfortunately, this hospital required no examination. At the end of approximately two years of employment, most of which time she had complained of considerable fatigue, she was transferred to a combined obstetrical and pediatric service. She was on this service only one and one-half days when she reported to a local physician for examination and chronic advanced tuberculosis with cavitation was found. Her sputum was teeming with tubercle bacilli. One of the infants born the first day she was on the service and to whom she gave intimate care developed mild respiratory symptoms at the age of six weeks and died of generalized miliary tuberculosis two weeks later. A careful search was made of all of the persons who had been in intimate contact with this child but none except the nurse was found to have tuberculosis in clinical form. The parents of the infant brought suit against the hospital with the thought that an institution is just as liable for having an employee who transmits a killing disease to a patient as an employee who unintentionally administers a lethal dose of a poisonous drug. The jury returned a verdict in favor of the plaintiff. The case was appealed and the Supreme Court upheld the verdict. Thus, the hospital was compelled to pay for the death of the child. It seems unfortunate that such catastrophies must occur in order to have our hospitals adapt a procedure which nurses and physicians have long known should be practiced everywhere.

In a school of nursing one has an opportunity to observe the tuberculous

infection attack rate among the students who react negatively to the tuberculin test on admission. Obviously, this rate will depend upon exposure to persons with tuberculosis in communicable form, whether or not it has been previously diagnosed.

Tables 1, 2 and 3 show the summary of tests on all nurses in Schools I, II and III. In figure 2 is illustrated graphically, the attack rate in the three schools of nursing and in a school of education over the period of 1929–1934 inclusive. In School I, it is observed that of all of the entering students over this period of years, 22.82 per cent reacted positively but on graduation 94.33 per cent reacted positively. Of all students entering School II from 1929–1934 inclusive, 23.88 per cent were positive on entrance but on

TABLE I

Summary of Tuberculin Tests on All Nurses in School I

Class Year	Number Enrolled	Entrance Test				Left Training				Graduation Test		
		Neg.	Pos.	Not Tested	Per Cent Positive	Neg.	Pos.	Not Tested	Total Number	Neg.	Pos.	Per Cent Positive
1929–32	31	17	11	3	39.29	5	4	3	12	—	19	100.00
1930–33	52	43	7	2	14.00	8	4	2	14	2	36	94.74
1931–34	35	22	12	1	35.29	5	6	1	12	1	22	95.65
1932–35	36	29	6	1	17.14	4	—	1	5	1	30	96.77
1933–36	31	27	4	—	12.90	6	2	—	8	2	21	91.30
1934–37	30	21	7	2	25.00	2	2	2	6	3	21	87.50
	215	159	47	9	22.82	30	18	9	57	9	149	94.33

TABLE II

Summary of Tuberculin Tests on All Nurses in School II

Class Year	Entrance Test			Left Training			Graduation Test		
	Number	Positive	Per Cent	Number	Negative	Positive	Number	Positive	Per Cent
1929–32	18	6	33.33	3	1	2	14	4	28.57
1930–33	41	13	31.71	13	10	3	28	12	42.86
1931–34	33	7	21.21	9	5	4	24	11	45.83
1932–35	22	5	22.72	5	3	2	21	12	57.14
1933–36	No class admitted for eighteen months								
1934–37	24	2	8.33	10	8	2	14	5	35.71
Total	138	33	23.88	40	27	13	101	44	43.56

TABLE III

Summary of Tuberculin Tests on All Nurses in School III

Class Year	Entrance Test			Left Training			Graduation Test		
	Number	Positive	Per Cent	Number	Negative	Positive	Number	Positive	Per Cent
1929–32	37	10	27.03	5	5	0	32	15	46.88
1930–33	53	13	24.53	11	9	2	42	19	45.24
1931–34	49	17	34.69	16	12	4	33	15	45.45
1932–35	55	16	29.09	10	7	3	45	14	31.11
1933–36	60	8	13.33	20	14	6	40	10	25.00
1934–37	38	5	13.16	12	9	3	26	4	15.38
Total	292	69	23.63	74	56	18	218	77	35.32

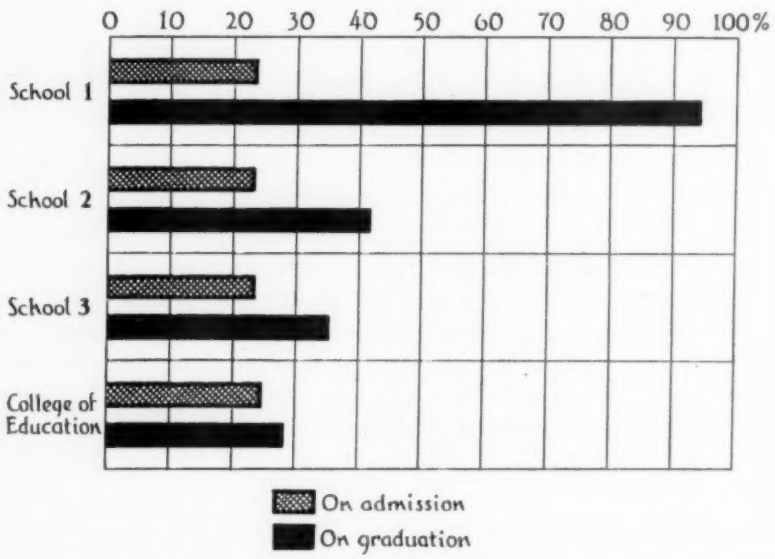

FIG. 2. Per cent of positive tuberculin reactors among student nurses and college of education students.

graduation only 43.56 per cent were positive. In School III, among the entering students from 1929–1934 inclusive, 23.63 per cent were positive; on graduation 35.32 per cent were positive.

The students entering the School of Education at the University of Minnesota were used as a control group because they are recruited from the same general communities and during their school years they resided in the same general environment. Here we see that among the students entering this school from 1929–1934 inclusive, 24.8 per cent were positive, while on graduation, 28.5 per cent were positive. The students in the School of Education take a four year course and, thus, were under observa-

tion one year longer than the students in the schools of nursing where the course is completed in three years.

During eight years of observation, we have frequently seen student nurses who reacted negatively to the tuberculin test on admission to school who later became positive reactors. In each case, we felt reasonably certain that there had been contact with persons who had tuberculosis in communicable form some time during the six months subsequent to the previous administration of the test. In seeking the source, some students knew of their exposure to tuberculous patients who had been in the hospital for diagnosis or treatment. Occasionally there was no such known exposure and we learned of co-existing tuberculosis in communicable form in the lungs of patients who had been in the hospital for other conditions, such as obstetrical care, fractures, and diabetes. Again, when no such source could be found we discovered that some hospital employee had communicable tuberculosis which may or may not have been previously diagnosed; at any rate its existence was not known to the hospital authorities. Thus, it was obvious that since the infection attack rate in each of these schools was greater than in a school of education in the same community, an attempt should be made to protect our students who had not been previously infected, against the first attack of the tubercle bacillus and those who came to us already infected, against reinfections.

While the later program did not permit girls in the schools of nursing to infect one another because of adequate examination and observation, they must be protected against exposure to others. In one hospital where the incidence of tuberculosis among the students and recent graduates had previously been high, we found a maid working in the kitchen and dining room who had far advanced chronic tuberculosis with a severe cough and an abundance of tubercle bacilli in the sputum. In another hospital we found an elevator operator who had sought this kind of work because of marked lameness. Our examination revealed that he had tuberculosis of the hip joint which had resulted in ankylosis. He also had extensive, chronic, pulmonary tuberculosis, not previously known to the hospital authorities. The student nurses and other members of the personnel were almost constantly using this elevator. In another hospital we found a librarian who had advanced pulmonary tuberculosis but who appeared well. Although she was under the care of a physician, the hospital authorities knew nothing about her disease. *In fact, the examinations of the non-professional personnel have revealed a number of cases of clinical pulmonary tuberculosis which in times past would have been permitted to continue in their work and spread tubercle bacilli to other members of the personnel.*

Any new discovery in medicine is usually slow to gain acceptance; therefore, because of this fact only in School I have we yet been able to convince the authorities that every non-professional employee should be carefully examined for tuberculosis when applying for work and if found free from tuberculosis in communicable form, annually thereafter. In this hospital

for the past two years, every employee has been carefully examined each year. In 1937, School II made the examination of non-professional employees optional. A number submitted but obviously the person who knows that tuberculosis exists will never consent to such an examination unless it is made compulsory. In School III, routine examination of non-professional employees has been considered but as yet they remain unexamined. It is of great interest to note that other hospital schools in the community now require annual examinations of all employees both professional and non-professional. The best example of this is the hospital operated by the University of Minnesota, where under the direction and leadership of Dean H. S. Diehl,[4] the students of nursing and medicine are no longer in danger of contracting first infections or reinfections from employees suffering from chronic pulmonary tuberculosis.

The statement has frequently been made that it is much more dangerous for members of personnel to work in general hospitals than on special tuberculosis services on the ground that in the former there may be patients with undetected communicable tuberculosis co-existing with other conditions for which they are being treated. However, our observations do not bear out this contention since in Schools II and III, which are general hospitals, it will be observed that the attack rate of tuberculous infection is considerably less than in School I, which is also a general hospital but has a special tuberculosis service. There is no question but that some cases of undetected tuberculosis spread their tubercle bacilli to the hospital personnel; in fact, we have seen a number of such cases. Although this is not as frequent a source of exposure as one sees on tuberculosis services, nevertheless, it has been of sufficient importance in our work to lead us to *recommend that every general hospital make a careful examination for tuberculosis in communicable form of every patient admitted to the institution regardless of the admitting diagnosis.* In none of the three schools here under consideration have we yet been able to convince the administrations or the medical staffs that such a procedure is essential to give the personnel adequate protection. However, under the direction of Dean H. S. Diehl for approximately two years the hospital of the University of Minnesota has provided adequate examinations for tuberculosis among entering patients. In this manner, a number of definite pulmonary lesions have been detected which without this special examination would not have been known to exist. This hospital operates a small tuberculosis service where patients found to have tuberculosis are admitted and treated for the condition for which they were sent to the hospital. Simultaneously their tuberculosis may be treated or if too advanced they are sent to a sanatorium as soon as the non-tuberculous condition has received adequate treatment. In any event a barrier is thrown up between the patient and the hospital personnel to prevent first infection or reinfection of those working in the hospital. In the Minneapolis General Hospital[5] beginning November,

1937, an order was issued to the effect that the tuberculin test is to be administered to every patient within 48 hours after admission and roentgen-ray examination made of the chests of all positive reactors.

Throughout our period of observation the greatest source of contamination of our students has been from known cases of tuberculosis; that is, patients who were on special tuberculosis services or who were being treated for tuberculosis in general hospitals which do not have special services. Frequently when a student reacted positively to the tuberculin test for the first time, she would actually mention the name of one or more patients known to have tuberculosis for whom she had cared in the hospital.

Obviously, when all hospitals examine their entering nurses adequately and periodically thereafter, when they examine periodically the entire personnel of the hospital, and when they examine for tuberculosis all entering patients, there should be no remaining source of contamination of personnel in the hospitals except from the patients known to have the disease.

The development of tuberculous lesions in the bodies of hospital personnel, particularly of professional students, has been discussed rather extensively during the past few years. Unfortunately, in a good deal of this discussion there has been no attempt to differentiate between the demonstrable primary complex usually free from significant symptoms, as it is visualized on the roentgen-ray film, and clinical reinfection type of tuberculosis. Obviously every student who enters a school with a positive tuberculin reaction and everyone who develops a positive reaction while in school has the primary tuberculosis complex somewhere in the body. Therefore, in every such person tuberculosis has entered upon at least its early phases of development. We have long since passed the time when it is logical to draw a sharp dividing line between tuberculous infection and tuberculous disease; we now look upon tuberculosis as a disease which begins when the neutrophiles first focalize tubercle bacilli. From this point it may pass through various phases of development over a long period of years or decades and eventually take the life of the individual. Again, at any point it may be brought under temporary or permanent control by the defense mechanism of the body.

When our report [1] was made in 1934, there was some discussion as to the significance of the tuberculin test having become positive in such a large percentage of students while in training. There were those who tended to minimize the situation. At that time our observations had not extended over a sufficiently long period of time to justify a report on the illnesses which had occurred among the students. Indeed, at present our observation period is only eight years for the first class studied and obviously it is impossible to draw any final conclusions regarding the remote hazards. However, we have already seen enough significant illness among these students to justify a preliminary report regarding the immediate hazards and the early remote hazards.

Although no attempt has been made to trace all of the students at this time, we contemplate such an effort and a statistical report at the end of approximately 10 years' observation. Suffice it to say that in School I, which had a tuberculosis service, there have come to our attention 10 girls who have developed reinfection forms of tuberculosis among the 215 who entered between 1929 and 1934, two of whom have already died. This is a definitely higher incidence than has come to our attention from Schools II and III and the School of Education.

Elsewhere [6] brief descriptions of the development of tuberculosis in the bodies of adults have been presented. They included not only those who had been observed in Schools I, II and III, at that time, but also some students who had been seen at the Students' Health Service of the University of Minnesota and elsewhere. We have since continued to make such observations and table 4 shows a summary of the cases.

TABLE IV

	Reaction to Tuberculin			Roentgen-Ray Findings	
	Number of Cases	Initial	Subsequent	Initial	Subsequent
Group I	2	Negative	Positive	Negative	Negative; had erythema nodosum
Group II	34	Negative	Positive	Negative	Parts of primary complex located by x-ray film
Group III	19	Negative	Positive	Negative	Pleural effusion with or without parts of primary complex located by roentgen-ray film
Group IV	27	Negative	Positive	Negative	Reinfection pulmonary tuberculosis
Group V	26	Positive	——	Negative	Reinfection pulmonary tuberculosis
Group VI	7	No record	Positive	Negative	Reinfection pulmonary tuberculosis
	115				

We have seen numerous tuberculous lesions develop in various parts of the bodies of our students who were infected in line of duty. For example, those who became positive to the tuberculin test and in whom we were unable to locate the lesion, while others presented such conditions as erythema nodosum, primary complexes in the lungs, pleurisy with effusion, cervical lymph node disease, bone and joint disease, epididymitis, peritonitis, tuberculous pneumonia, and chronic pulmonary tuberculosis which reached such proportions as to take the lives of our former students years after they had graduated. In some cases, only one demonstrable lesion has

come to light; in others multiple lesions have made their appearance as the years have passed (figure 3). Practically the only significant lesions we have not seen among our students are those of miliary tuberculosis and tuberculous meningitis.

We desire to reëmphasize the fact that when adults become infected for the first time in life they develop the primary tuberculosis complex as do infants and children. This is contrary to the former belief which we have never been able to substantiate by actual observation that a person

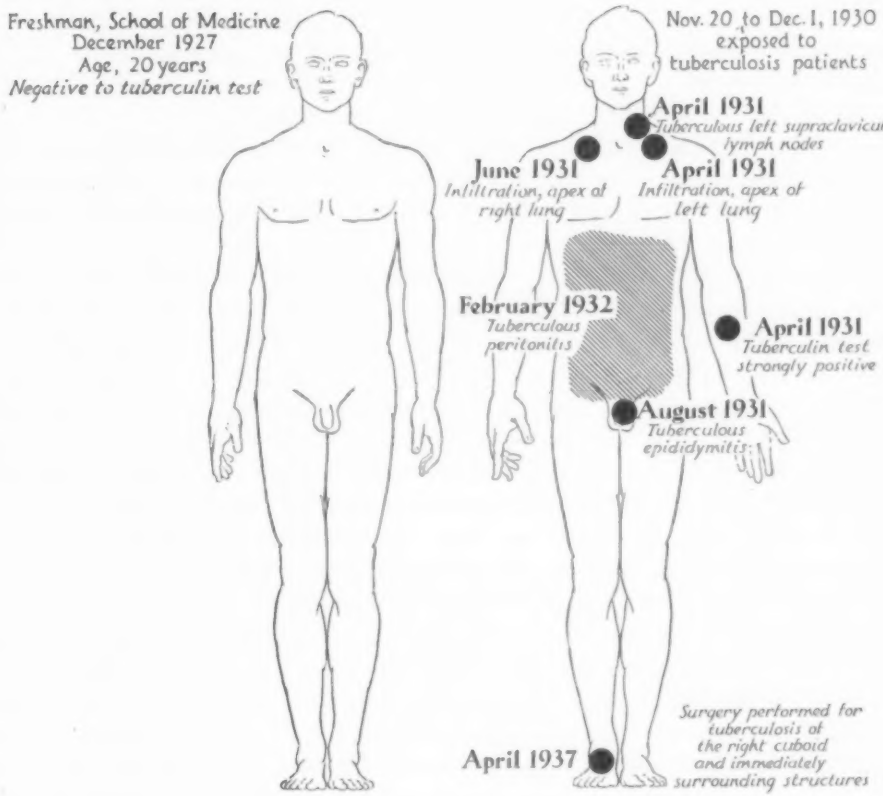

FIG. 3.

who does not become infected with a so-called immunizing dose of tubercle bacilli in infancy or childhood has very little chance of survival if infected in adult life. Over the past decade we have seen large numbers of students of nursing and medicine who reacted negatively to the tuberculin test on admission to schools but who following exposure to patients with tuberculosis developed a high degree of allergy, indicating the presence of primary tuberculosis complexes in their bodies. The majority of them had no symptoms and would not have known that tuberculous lesions were

present had it not been for periodic tuberculin testing. Moreover, roentgen-ray films of the chest remained clear. In a minority group who became positive to the tuberculin test under our observation, parts of primary complexes were located by roentgen-ray film but these persons were as free from symptoms as others in whom the location of the primary complex was not determined by roentgen-ray film or any other phase of the examination.

A review of the cases presented reveals the fact that there is usually an interval of months or years between the development of the primary complex and destructive lesions of the reinfection type. Indeed, only a few of the persons whose infection in adult life we have observed have yet fallen ill or have developed the reinfection type of lesions which have required treatment in the presymptom stage. However, because of the presence of foci of tubercle bacilli in their bodies, we look upon every one who has developed the primary complex under our observation as a potential case of a destructive type of tuberculosis, just as those who already had evidence of the primary complex, manifested by the positive tuberculin reaction, when they first came to us.

There is extant the term "infantile" tuberculosis which seems to cause even physicians to shudder when it is mentioned. This condition is said to be directly due to the first infection with tubercle bacilli, which is highly destructive among infants—hence the name. It is frequently mentioned in connection with deaths from tuberculosis among persons of primitive races and is said to be the type of disease which is likely to develop if first contact with tubercle bacilli is postponed to adult life among members of the Caucasian race. From a careful perusal of the literature, we have become firmly convinced that the term "infantile" tuberculosis is a misnomer and that it is a myth as far as adults are concerned. From descriptions in the literature, it appears very definite that the term "infantile" tuberculosis has been applied to those infants who have developed tuberculous meningitis, tuberculous pneumonia, and miliary tuberculosis, all of which are acute reinfection forms of disease and appear only in the bodies of those who are developing or have developed the primary complex, from some part of which tubercle bacilli have escaped into a bronchus or one of its ramifications, a blood vessel, a ventricle of the brain, or the subarachnoid space. Although we are thoroughly cognizant of the fact that such happenings may occur to any one of the group of adults under our observation, we have not yet seen a single case of meningitis or miliary disease among them, and tuberculous pneumonia has appeared with rarity. The number we have observed is sufficiently large so that certainly if the highly destructive so-called "infantile" form of tuberculosis is as common among adults who first become infected as one would be led to believe from opinions expressed in the literature, we would already have seen many such cases; to date we have not seen one.

Heimbeck's articles and personal communications lead us to believe

that the student nurses whom he has had under observation have had experiences almost identical with those of our group. In 1936, he [7] reported 280 students who had become positive to the tuberculin test while under his observation, all of whom, of course, had primary complexes somewhere in their bodies and in 96 of whom he reported evidence of disease determined by other phases of the examination. Among the 96 cases there were 39 who in addition to the positive tuberculin reaction had erythema nodosum as the only other manifestation of the disease. The roentgen-ray films of their chests were entirely clear. This condition has appeared much less frequently in our group than in Heimbeck's student nurses. While we appreciate the fact that erythema nodosum may accompany the development of tuberculosis, particularly when a high degree of allergy is present, we also recognize other causes of this condition and, therefore, cannot always say with certainty that it is a manifestation of tuberculosis. In Heimbeck's 96 cases, 26 were classified as having had only pulmonary infection or enlargement of the hilum lymph nodes. From his descriptions of these cases, we believe that they have the same type of lesion as those in our Group II, table 4; that is, evidence of the location of the primary complex was revealed by the roentgen-ray film examination. Sixteen of Heimbeck's cases had only pleuritis. Only 13 of his 96 cases have developed clinical pulmonary tuberculosis throughout the period of observation, such as those we have reported in Group IV, table 4. Among the 96, Heimbeck has had two fatal cases of tuberculous meningitis. Thus, it would appear that only 15 of his 96 cases have developed serious lesions subsequent to the appearance of the primary complex, 13 of whom had the ordinary variety of pulmonary tuberculosis.

It has been intimated that the adults who have been observed to develop positive tuberculin reactions probably were infected with tubercle bacilli as infants or children and later lost their allergy but retained their immunity, so most of them have tolerated well their infections received while under our observation. Therefore, they are unlike adults of primitive races who have never previously been infected. We have been unable to find any evidence to substantiate such belief since in the community where our work was done the infection attack rate among infants and children,[8] as well as young adults, is approximately 1 per cent each year (figure 2). Moreover, it has not been shown that a very high percentage of children and young adults lose their allergy to such an extent that it cannot be detected by the tuberculin test. Furthermore, roentgen-ray films of the chests of negative reactors have not revealed even the small percentage with calcifications which one might expect to see in a group who had previously developed primary complexes.

The above findings lead us to the all-important subject of protecting students of nursing and medicine and other members of the hospital or sanatorium personnel. *When we allow members of either the professional*

or non-professional personnel of a hospital to take into their bodies for the first time, tubercle bacilli, a serious situation is created inasmuch as we have no way of permanently desensitizing their tissues and no therapeutic measure that will destroy the tubercle bacilli which we have allowed to set up foci of disease. In short, each person who becomes positive to the tuberculin test has developed in the body manufacturing plants of tubercle bacilli from which endogenous reinfection may subsequently occur. Moreover, as long as their tissues remain allergic they may be in danger of necrotizing lesions developing should they become reinfected from exogenous sources. Although it requires the remainder of the span of life of these persons before one can recount all of the damage done to their bodies through the first infection with tubercle bacilli obtained in the hospital, already the morbidity and mortality among such persons is a sad story to relate. Moreover, one cannot overlook the fact that we are graduating nurses and physicians to serve the general public in the most intimate relationship of any professional group and are contaminating them with a disease which we are trying to train them to combat; in fact, we are perpetuating foci of tubercle bacilli at the most vulnerable point of modern life. Many persons have contracted tuberculosis from nurses who developed the beginning of their disease while in training. Now that the gravity of the problem of tuberculosis among the hospital personnel, particularly professional students, has been generally recognized the solution is of extreme importance. A number of suggestions have been made by various persons with the thought of reaching a solution. Some of them are as follows:

1. *That only older girls be permitted to take tuberculosis services while in training and that only older graduate nurses and non-professional workers be employed in sanatoriums and on tuberculosis services of general hospitals or in single rooms in general hospitals which admit tuberculous patients.* In fact, some workers have set the minimum age limit at 25 or 26 years and some schools of nursing have reserved the tuberculosis service for the senior year. Recent observations have shown that the human body will become infected with tubercle bacilli whenever sufficiently exposed whether it be in infancy, senility, or at any intervening time. Thus, our previous viewpoint with regard to all tuberculosis beginning in childhood or young adult life was not founded on fact. There is now an abundance of evidence to show that persons beyond the age of 25 years not only become infected for the first time in their lives but also develop demonstrable clinical lesions. In fact, we have known for a long time that there is far more clinical tuberculosis in persons in the third and fourth decades of life than in the second; therefore, we have no evidence that the admission of girls as students or graduates to tuberculosis services or the employment of professional workers after the age of 25 years, would be of any aid whatsoever in solving the problem.

2. *That we admit to schools of nursing or employ on tuberculosis services only those who react positively to the tuberculin test.* The only difference as far as the development of clinical tuberculosis is concerned between such a group and those who react negatively is that for the most part the positive reactors have usually passed through the immediate hazards but the remote hazards are identical and it is these that are far more significant to the individual and to the perpetuation of tuberculosis in a family or a community. There is now evidence to show that students and graduates of nursing who enter with positive tuberculin reactions later fall ill in considerable number from clinical forms of disease (group V, table 4). Moreover, if one were to limit the admissions to our schools of nursing only to girls who react positively to the tuberculin test, already in many parts of the country it would be impossible to find enough such girls interested in nursing to complete the desired enrollment for each class. For example, in figure 2 it is seen that of all the girls entering three schools of nursing from 1929 to 1934 inclusive, an average of slightly less than 24 per cent reacted positively. Obviously, in a school of nursing admitting 100 students to the first year class more than 400 applicants would have to be examined in order to secure 100 with positive reactions. With the incidence of positive tuberculin reactors definitely decreasing a much larger number would need to be examined. For example, in figure 1 it is observed that less than 5 per cent of the students entering Schools I and II in 1935 reacted positively to the test. On this basis it would be necessary to examine more than 2,000 students in order to find one hundred who would qualify on the basis of the positive tuberculin reaction. Moreover, schools of nursing would be compelled to accept any type of student regardless of those important qualities of a nurse, such as personality, scholastic attainment, etc. Inasmuch as tuberculosis has become a compensable disease in some of our states and will probably be so regarded and dealt with throughout most of the country within the next few years, one can readily see why those in charge of an institution might desire to enroll or employ only professional and non-professional workers who react positively to the tuberculin test. All evidence of infection which might occur in the institution is obscured by the presence of the previously positive reaction. There would be no way of determining with accuracy the liability of the institution, whereas, when members of the personnel first become infected in an institution, the tuberculin test provides all the evidence needed by Industrial Commissions and the courts to place the responsibility. It is far better to face the situation and solve the problem than to enter long and expensive litigations.

3. *That it is better for students to become contaminated with tubercle bacilli while in a hospital or sanatorium where they can be carefully observed and given good care.* This argument might suffice in diseases of fixed short incubation time, such as typhoid fever and diphtheria, when the

student would actually remain in the institution until the attack is over, but it can never be considered a sane argument for a disease like tuberculosis in which there is no fixed incubation time and most persons who contract it are not ill until many months or even many decades after they have completed their tuberculosis services. Indeed, the greatest destruction occurs after the students graduate.

4. *That it is good for student personnel to contract their first infection type of tuberculosis while on duty on special tuberculosis services in general hospitals and in sanatoriums because of the small dosage they receive.* We are dealing with a microörganism; we do not see the bacilli when they enter the body; we have no way of counting them; moreover, we have no method of determining whether a student has received a small or a large dose. Certainly, one cannot overlook the fact that tubercle bacilli are alive and are capable of multiplying so that a single bacillus may develop into a large colony in a short time. Indeed, Corper [9] has shown that when from one to ten bacilli are planted on culture media under ideal growing conditions in the laboratory, they have multiplied to one billion in three to four weeks. This fact should be most discouraging to us even if we were able to absolutely control dosage.

5. *That it is an asset for the student of nursing or medicine to become infected with tubercle bacilli, as such infection affords adequate immunity.* In the light of recent observation, such a viewpoint is obsolete. Clinicians who have made careful observations are aware of the fact that immunity which may result from the development of the primary tuberculosis complex is not dependable. For example, Burrell [10] says: "But with tuberculosis there can be no question of getting from a first infection an immunity in any way comparable to that obtained by smallpox, mumps, or scarlet fever." Chadwick [11] says: "There is without doubt a slight amount of immunity conferred by an infection with the tubercle bacillus, provided it is not excessive and the child has an average amount of resistance. However, it is important to remember that this immunity cannot be depended upon to prevent disease." To state that a primary tuberculosis complex protects against subsequent development of destructive forms of tuberculosis of various parts of the body is comparable to stating that a primary syphilitic lesion protects against the development of destructive lesions in various parts of the body. The microörganisms of these two diseases are similar in respect to their ability to survive over long periods of years in the human body. It is a well known fact that approximately two-thirds of the persons who develop primary syphilitic lesions never fall ill from the disease but the remaining one-third, years or decades later, develop such conditions as paresis, tabes dorsalis, aortitis, etc. Among those who develop primary tuberculous lesions, probably 75 per cent never fall ill from destructive forms of the disease but evidence is now accruing [12] which is pointing toward an incidence of at least 25 per cent of clinical lesions in the lungs, kidneys,

bones and joints, meninges, etc., years or decades following the development of the primary lesion. Our observations at Lymanhurst and at the University of Minnesota lead us to strongly suspect that many of the reinfection type of lesions are the indirect result of the presence of the primary lesion just as is true in syphilis. Moreover, we do know that in an experimental way, lesions can be developed in the bodies of the previously infected by the introduction of tubercle bacilli from exogenous sources. Therefore, the exogenous source of the reinfection form of at least pulmonary tuberculosis can by no means be ignored.

6. *That all nurses and physicians and non-professional members of the hospital personnel must sooner or later become infected with tubercle bacilli; therefore, the sooner the infection occurs the better.* This does not appear to be based on sound reasoning because it is only after infection occurs that the individual becomes a potential case of clinical tuberculosis; in other words, where there are no tubercle bacilli there can be no tuberculosis. Moreover, the chances of the graduate in nursing and medicine becoming infected outside of tuberculosis services are rapidly decreasing; in fact, in figure 2 we see that among the students in a school of education residing in the same general community the increase in the infection attack rate is approximately 4 per cent in four years; in other words, about 1 per cent become infected each year. There is reason to believe that even this low attack rate will definitely decrease in the next few years. Even with an annual increase of 1 per cent, it would require one hundred years before one hundred infants being born this year and remaining in the general population would all be infected with tubercle bacilli for the first time. We now have evidence that in some parts of this country only about 5 per cent of the girls and boys have been infected with tubercle bacilli even in the high school age period. Here the attack rate is only about ⅓ of 1 per cent per year. Thus, it is obvious that the chances of the nurse or the physician becoming infected or reinfected through association with the general public even in the practice of their professions are not great.

7. *That the professional and non-professional members of the personnel working on a tuberculosis service know that all the patients have tuberculosis and, therefore, are in less danger than while working in a general hospital where the occasional patient may have this disease in unsuspected but communicable form.* Our observations as shown in figure 2 do not bear out this contention, since in Schools II and III without tuberculosis services the infection attack rate was far less than that in School I with a tuberculosis service. Because of the insidiousness of tuberculosis, the inexperience of students, and their lack of perspective, it is well nigh impossible in that stage of their professional career to convince them of the dangers of exposure. Furthermore, it is impossible to secure adequate coöperation of all patients on tuberculosis services which would guarantee adequate protection of the students. The majority of patients have had no training in com-

municable disease control, and therefore, do not understand the fundamentals. The occasional patient is subnormal mentally and some are too ill to maintain any protection whatsoever of the personnel. In reality it makes no difference whether human beings come in contact with tuberculosis in the home, in the general hospital, in the sanatorium, or elsewhere; if tubercle bacilli are allowed to pass from patient to personnel, there immediately develops a health liability. The fact that the tuberculous patient is taken from the home to a tuberculosis service in a hospital or a sanatorium has no influence on the virulence of the bacilli nor does it change the method of transmitting the disease.

8. *That attempts be made to immunize all student members of the personnel against attacks of virulent tubercle bacilli from the patients with whom they come in contact.* Ever since the discovery of the tubercle bacillus, much thought, time and effort as well as large sums of money have been spent on methods of immunization. Indeed, tuberculin was first thought to have an immunizing effect. Numerous vaccines have been prepared and extensively employed but all have fallen or are rapidly falling into disuse because of their ineffectiveness. Dead tubercle bacilli have been used to prevent tuberculosis by such persons as Arima,[13] Zadek and Meyer,[14] but without significant results. Living virulent tubercle bacilli have been introduced into the bodies of animals and human beings by such persons as Kutschera-Aichbergen [15] in attempts to immunize against tuberculosis. Acid-fast bacilli from cold-blooded animals, particularly the turtle, have been extensively employed by such persons as Friedmann [16, 17] and Fowler.[18, 19] These various attempts to immunize the human body against tuberculosis had their day when many persons became enthusiastic and exhorbitant claims were made. They held the center of the stage for a time and then vanished, leaving no trace of good to humanity except the knowledge that they had failed. In more recent years, Calmette [20] and his disciples have been in the limelight with BCG. Many hailed the announcement of this material as the product of a new thought, when in reality the thought is as old as the scientific study of tuberculosis itself. BCG represents an old method in a slightly different garment. It is reported that this material has been introduced into the bodies of more than a million persons in Europe alone. It has also been employed in a large way in an attempt to control tuberculosis among the animal herds. The results from different parts of the world from both the veterinarians and those working in human medicine are extremely conflicting. For example, where BCG has been used to control tuberculosis in animals some workers have reported excellent results; on the other hand, in this country where it has been given ample trial, it has been condemned and the veterinary profession does not consider it of any value in the tuberculosis control program among cattle. In the work among human beings, some authors are very enthusiastic, claiming reductions in the acute fatal forms of the reinfection type of disease in infants; others

manifest no enthusiasm whatsoever after giving it what they consider adequate trial.

No one has yet kept under close observation, a group of persons to whom BCG was administered in infancy, together with a control group, through that period of adult life when tuberculosis is most destructive in the human family. The fact that there is so much disagreement in results obtained by various workers tends to militate against the use of BCG. Moreover, deaths reported and illnesses occurring among persons who have supposedly been immunized by this method apparently are causing enthusiasm to wane in Europe. For example, the death of an infant previously vaccinated with BCG in Paris, the birthplace of this substance, resulted in a discussion [21] which reflects the marked decrease in confidence; the belief was expressed that infants should be separated at birth from tuberculous parents and kept away from them as long as possible, preferably for at least a year. This precaution, they said, is just as necessary with vaccinated as with unvaccinated infants. Commenting on this incident editorially, the British Medical Journal states [22]: "Whatever the ultimate value of BCG will be found to be in practice, it is certain that reliance on its efficacy to the exclusion of general prophylactic measures will lead to nothing but disappointment." Apparently, therefore, it becomes a matter of preventing virulent tubercle bacilli from entering the body through isolation, rather than the introduction into the body of BCG, which will demand the emphasis in the future. It is not at all unlikely that the apparent good results reported by some authors have been due to isolation rather than BCG. Excellent results have been reported by workers such as Grancher [23] and Bernard [24] from the employment of isolation alone.

It seems somewhat paradoxical that as the enthusiasm for BCG is beginning to wane in Europe where it has been most extensively used, an enthusiasm for its use should be developing in this country. There are those who are now advocating it as a solution of the problem of tuberculosis control among hospital personnel. This is largely on the basis of Heimbeck's work in Oslo, which on careful analysis would hardly seem to justify any enthusiasm.

If we were to administer BCG to all professional and non-professional members of the personnel of our hospitals in such dosage as to produce allergy, we would immediately blot out our most valuable diagnostic procedure in tuberculosis, namely, the tuberculin test. If it were employed only among students of nursing and medicine in our institutions where studies of the transmission of tuberculosis are in progress or might be undertaken, there would remain no way of determining whether there was a spread of tubercle bacilli from the patients to the personnel. Certainly even though we had a method of immunization of proved value, still we would not desire to have tubercle bacilli spread from patient to student. With an immunization as effective as that now in practice in diphtheria, we still

protect the personnel against contamination with diphtheria bacilli through isolation technic.

9. *That strict contagious disease technic be instituted wherever persons with communicable tuberculosis are treated.*

Inasmuch as we know that tuberculosis is always caused by the tubercle bacillus, we know how this organism is transmitted from person to person and we have no method of immunization of proved value despite numerous attempts, the only logical procedure in the protection of our students of nursing and medicine or graduates in these professions who are compelled to take or choose work on tuberculosis services is to throw up a barrier around the patient which will prevent the spread of tubercle bacilli to the bodies of those who care for him.[26] This has been done so successfully in typhoid fever and diphtheria that it is difficult to comprehend a viewpoint which denies the possibility of the success of such a procedure in tuberculosis.

It is true that most of our sanatoriums for the tuberculous are not equipped to institute strict contagious disease technic and a considerable expenditure of money would be necessary to equip them. However, the question is being asked and justifiably so as to whether it is more reasonable to make the necessary expenditures or to allow the great sacrifice in health and life to continue among students and graduates of nursing and medicine. Already in a few places attempts have been made to protect professional workers against tubercle bacilli eliminated from the bodies of their patients but for the most part these attempts have been feeble. They have consisted of a modified contagious disease technic which has failed. In 1933, attention was called [25] to the fact that while such experiments constituted a laudable attempt and a definite step forward, the technic was in no way comparable in its execution to that employed on diphtheria services and, therefore, it could never succeed. *The school of nursing which insists upon a tuberculosis service for its students can no longer justly do so without insisting upon the establishment of a strict contagious disease technic where the students are to be taught, whether it be in a general hospital or in a sanatorium.*

All of our larger hospitals should have tuberculosis services or better include this service with the general contagious disease service where patients can be admitted to protect the communities from which they come and other patients in the hospital against the spread of their tubercle bacilli. If an adequate contagious disease technic is then established on such services and in our sanatoriums, there could be no objection to students of nursing and medicine being taught their contagious technic on such services. Since most of our sanatoriums are so constructed that it is impossible to immediately establish contagious technic throughout and while appropriations are being sought and the necessary changes are being made, small units can be set up for the teaching of students where contagious disease technic in its strictest form can be employed. Although this has frequently been pro-

posed, it has been objected to on the ground that students are needed to do work about the institutions. If such work could be done by others and the time the student spends on the tuberculosis service could be limited entirely to teaching, all of the actual instruction which students now receive could be given in a brief period of time.

It has been argued that tuberculous patients would object to the institution of strict contagious disease technic. After many years of intimate association with large numbers of tuberculous patients, we cannot possibly concur in this belief. There is no finer group in American society; it is a cosmopolitan group, as its members come from every walk of life; they constitute a most reasonable and thinking group and must be numbered among the best educators in the campaign against tuberculosis. Not infrequently when an individual is first told that tuberculosis exists in communicable form, the first expressed thought is with reference to the harm that might have been done to his associates; the second is, what can be done to protect these associates in the future? A part of the patient's training should be in contagious technic and by seeing this practiced, indeed, in helping to practice it, invaluable lessons are learned which he can apply while on treatment and thereafter.

10. *That the student personnel, particularly nurses, be prevented from coming in contact with patients who have tuberculosis in a contagious stage.* This method is simple in its execution. To have it succeed every member of the professional and non-professional hospital personnel must be kept under close observation; every patient entering the hospital must be examined for communicable tuberculosis. In other words, an environment must be created which is free from liberated tubercle bacilli. This should guarantee students an infection attack rate no greater than that prevailing in the general public where they are working.

If student nurses are prevented throughout their course from having contact with tuberculous patients, the question immediately arises as to the importance of tuberculosis training for nurses. We have come to believe that the necessity for such training has been greatly over-estimated, although a decade ago, before its dangers to students were fully appreciated, one of us [27] was among its most enthusiastic supporters. After all, the nursing care of the tuberculous patient does not differ from that of patients on general medical or surgical services, except that tuberculosis is contagious. Certainly every nurse should have training in strict contagious disease technic and at present in most places this is given safely on services admitting patients with such diseases as diphtheria. If after graduation the nurse is called upon to care for the occasional tuberculous patient, the technic she has learned on a contagious disease service, including the long time observation of diphtheria carriers, is adequate to protect her against tuberculosis.

In the light of our modern knowledge of tuberculosis it appears unfor-

tunate that a course of training in tuberculosis is necessary to bring a school of nursing to the standard which some ambitious supervisors desire to have their schools attain. In fact, some have placed the standards of their schools high at a terrible sacrifice in the future health and even life of their students, not only during the short period of training but for all subsequent time. Fortunately, the number of supervisors who have such ambitions and have realized them apparently is small. McNett [28] states that only 10 per cent of the schools of nursing of the United States now offer instruction and experience in tuberculosis and probably not more than 2 or 3 per cent actually give organized courses.

Indeed, we believe the problem of tuberculosis nursing will best be solved when we employ in our sanatoriums and tuberculosis services in general hospitals, only graduate nurses. We have in mind not only the nurse but also the patient. Certainly the best trained nurses are none too good for the tuberculous patients. The problems of the patients are serious ones; their stay in the hospital often is long and we are not doing them justice when we employ untrained persons to care for them.

Tuberculosis nursing should become a specialty just as anesthesia, obstetrical, pediatric and surgical nursing have become specialties. After a general course has been completed in nursing, those who choose to work in institutions and on services for the tuberculous *should take special training in this field. Their compensation should be commensurate not only with their expertness but also with the hazard of their environment.* When the situation is dealt with in this manner, we will no longer risk the health and all too often the lives of nurses compelling them as undergraduates to take tuberculosis services. Students have not reached such maturity or have not had experience enough to have the proper perspective with regard to the dangers of tuberculosis.

We no longer have the excuse of an unrecognized or invisible danger. We have found the problem by accumulation of the inescapable facts, and we are thereby forced to provide the solution.

Summary

1. Since 1929 entering students in three schools of nursing and one school of education have had the tuberculin test administered. Of all the students entering these schools from 1929 to 1934 an average of approximately 23 per cent have reacted positively on admission. The incidence of positive reactors among the probationers has definitely decreased in the more recent years of this study.

2. All students in the schools of nursing who react negatively to the tuberculin test are retested every six months as long as they remain negative.

3. In each of the schools of nursing the incidence of positive reactors definitely increased before graduation. In one school the increase was from 23.63 per cent to 35.32 per cent; in another school the increase was

from 23.88 per cent to 43.56 per cent; while in a third school the increase was from 22.88 per cent to 94.33 per cent. In the school of education the increase was from 24.8 per cent to 28.5 per cent.

4. Roentgen-ray films of the chest have been made of positive reactors on admission to determine the presence or absence of shadows which might be due to pulmonary tuberculosis in an attempt to detect disease requiring treatment or in a communicable form.

5. Those students in the schools of nursing who became positive to the tuberculin test under our observation have then had roentgen-ray films made of their chests, the same as those who entered with positive reactions, and films were made annually thereafter as long as they remained in the school.

6. Tuberculous primary complexes developing among student nurses, as manifested by the positive tuberculin reaction, were sometimes traced to other members of hospital personnel. Therefore, we have strongly recommended that all persons employed in the hospital regardless of their capacity be adequately examined for tuberculosis. Where this has been done definite cases have been found.

7. Most frequently primary complexes were traced to patients who had communicable pulmonary tuberculosis. Some of them had entered the hospital because of tuberculosis; some were admitted for other conditions but previously unsuspected pulmonary tuberculosis was present. The latter group has caused us to strongly recommend that every patient entering a hospital, regardless of the admitting diagnosis, be adequately examined for pulmonary tuberculosis in communicable form. Where this procedure has been carried out, it has more than justified time and expense. When persons are found to have communicable pulmonary tuberculosis co-existing with the condition for which they entered the hospital it is recommended that they be isolated in the institution and treated for both conditions.

8. By examining all student nurses on admission to school and periodically thereafter, by making adequate examinations of all other members of the personnel, by examining every patient on admission to the hospital, and by isolating and treating all persons in each of these groups found to have communicable tuberculosis, the hospital environment can soon be made safe from the standpoint of contracting tuberculosis. When such a program is in effect, members of the personnel should not show any higher incidence of positive tuberculin reactions or of clinical disease than persons in the general population employed elsewhere.

9. An adequate examination for members of the personnel, as well as entering patients, consists of the tuberculin test and roentgen-ray films of the chests of the positive reactors. These two procedures serve only as screens for from them alone one cannot make a final diagnosis. Those with shadows on roentgen-ray films must have careful clinical examinations including laboratory work and not infrequently the bronchoscopist must be called in consultation.

10. Every member of the hospital personnel who reacts positively to the tuberculin test upon employment or subsequently becomes a positive reactor has developed the primary tuberculosis complex. However, in the majority of such persons the tuberculin test is the only evidence which can be obtained prior to a postmortem examination. In a small percentage, the roentgen-ray film has aided in determining the location of parts of the primary complexes.

11. The main object of this study is to determine the best method of preventing the spread of tuberculosis from one member of the personnel to another, from personnel to patient, and patient to personnel. So far as student nurses are concerned such factors as age, positive tuberculin reactions on admission, dosage of tubercle bacilli, etc., have been discussed but none of them appears to be of any avail.

12. Attention is called to attempts to immunize student nurses against tuberculosis but no method has yet been devised which has been proved to be both safe and efficacious.

13. For those schools which continue to demand that their student nurses take a tuberculosis service, strict contagious disease technic, such as that which has been found effective in other contagious diseases, is strongly recommended.

14. The safest procedure from the standpoint of the student nurse is to keep her from coming in contact with tuberculous patients while in training. This can be done with no particular loss to her future efficiency as a nurse. We believe that only graduate nurses should be employed on tuberculosis services, both in hospitals and sanatoriums, and that such nurses should take graduate training in the fundamentals of tuberculosis before engaging in the active care of patients. Moreover, the compensation of such nurses should be commensurate with their expertness in this field, as well as the hazard of their environment.

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ACID–BASE WATER BALANCE*

By Edward C. Mason, M.D., Ph.D., F.A.C.P., and Arthur A. Hellbaum, M.A., Ph.D., *Oklahoma City, Oklahoma*

Under certain abnormal conditions, the body tissues hold an abnormally large amount of water (edema), and this increased hydration of the tissues most frequently accompanies impairment of the blood circulation. One of the functions of the blood is to carry waste products (solid, liquid, and gas) from the tissues; the most obvious of these is the transport of carbon dioxide. If carbon dioxide is allowed to accumulate in the presence of water, the result is the formation of carbonic acid. Studies conducted on excised organs and other colloids have revealed the fact that acid produces a marked increase in their hydrophylic properties. This is evidenced by their marked swelling and increased water content. Therefore, it has been reasoned that the accumulation in the tissues of stagnant, unaerated blood allowed the accumulation of acid and caused the increased hydration capacity of the tissues.

With a knowledge of the above facts and the interpretation of his experimental data Martin H. Fischer has offered an extremely logical explanation of tissue hydration. His interpretations are ably presented in his book "Oedema and Nephritis,"[1] in which he states,[2] "*In consequence of circulatory disturbances, whether general or local, an abnormal production and accumulation of carbonic, lactic and other acids occurs which increases the hydration capacity of the colloids of the involved tissues, because of which they then suck water out of the blood and lymph streams bathing them.*" He has also called attention to the fact that diuretics, such as caffeine and digitalis usually act by improving the circulation of the blood, the better circulation providing better aeration (carbon dioxide elimination), more free water, better secretion and better excretion.

Hyperventilation and Water Balance

While studying the factors active in producing the morning alkaline tide Leathes in 1919[3] focused his attention on the part played by respiration. He concluded that respiratory activity could markedly affect the reaction of the urine. While his chief interest was in the reaction of the urine, his data also show a very marked increase in urine production during hyperventilation. His results show that 20 minutes of hyperpnea caused an urinary increase from 56 c.c. per hour to 123 c.c. per hour, and an increase of alkalinity from 36 per cent to 91 per cent.

Collip and Backus, 1920,[4] confirmed the observations of Leathes and in addition determined the changes produced in the carbon dioxide tension of

*Read before the American Physiological Society, Baltimore, Maryland, April 2, 1938.
From the Department of Physiology, University of Oklahoma, School of Medicine.

alveolar air, carbon dioxide combining power of the venous plasma and the acidity of the urine—before, during and after periods of hyperpnea. They also determined the rate of excretion of phosphates, ammonia and water by the kidneys during these periods. A summary of their observations includes the following: "The average fall in carbon dioxide tension of the alveolar air was 44 per cent. The average fall in carbon dioxide combining power of the venous plasma was 14.3 per cent. The acidity of the urine was markedly decreased. A diuresis was noticed. The rate of elimination of phosphates was increased." Their data demonstrate that, in one case, hyperventilation for 32 minutes caused an increase in urinary output from 46 c.c. per hour to 220 c.c. per hour. Several of their other subjects also showed a marked diuresis accompanying hyperpnea.

Administration of Alkali and Water Balance

"In prolonged hyperpnea one finds that the kidney responds in much the same manner as it would if the subject had received a large dose of sodium bicarbonate by mouth or by intravenous injection" (Collip and Backus [4]). This statement is in complete accord with the explanation previously offered by Martin H. Fischer and is the foundation of his treatment of "Oedema and Nephritis." Since hyperventilation (carbon dioxide elimination) yields more free water, better secretion and better excretion, it has been considered logical to assume that the same result could be accomplished by the administration of sodium bicarbonate. *Our experience does not confirm this assumption.*

We have repeatedly observed a marked and sudden gain in weight of patients who have received sodium bicarbonate, and this has prompted us to continue the observations.

Experimental

We have collected the following data on 54 normal subjects: (1) the pH of the morning urine before administering sodium bicarbonate, (2) the body weight before ingesting 36 grams of sodium bicarbonate (4 grams t.i.d. for three days), (3) the pH of the urine the morning of the fourth day, (4) the body weight the morning of the fourth day, and (5) the body weight three days after the test.

The data thus obtained are too extensive to submit in their entirety and therefore we have summarized our findings as follows:

Weight Changes in 54 Subjects Receiving Sodium Bicarbonate

I. *Increased weight:* 49 subjects gained a total of 111.75 pounds, the greatest gain being 6.5 pounds, and the least 0.25 pound.

II. *Decreased weight:* 2 subjects lost a total of 2 pounds. These two were the only individuals in the group weighing above 200 pounds (217½ and 216½); one developed a diarrhea.

III. *No weight change:* 3 subjects showed no weight change during the three day period.

IV. *Weight three days following test:* All weights had returned to approximately normal at the end of three days after completion of test.

V. *pH changes:* Measurements by the Beckman pH meter (glass electrode) showed an increase in the pH of the urine in all subjects, the usual increase being approximately from 1 to 2 pH units; one subject had an increase of 2.20. The degree of increase in pH of the urine did not correspond to the degree of weight gain.

Effect of Calcium Chloride and Other Acid Forming Salts

According to the Hofmeister series and the observation of colloidal chemists, including Fischer, the calcium stearate is much less hydrated than the sodium stearate (soap). Likewise calcium-tissue compounds are less hydrated than the sodium-tissue compounds. Therefore it was reasonable to assume that if one could replace sodium (which caused high hydration) by calcium, the tissue would be less hydrated and yield free water.

That the calcium salts are effective in the treatment of edema is abundantly demonstrated by the work of Meyer and Cohn [5] 1911, Schultz [6] 1918, Hülse [7] 1920, Rockwood and Barrier [8] 1924, Keith, Barrier and Whelan [9] 1924.

Haldane and his co-workers,[10] 1921, studied the action of calcium chloride diuresis and observed an acidosis, fall in alveolar carbon dioxide, increased excretion of sodium, ammonium and total acids of the urine, with a reduction in its hydrogen-ion concentration. They explained the diuresis as being due to the acid reaction of calcium chloride, and that such acid brought the tissue proteins nearer the isoelectric point. On this basis they predicted that ammonium chloride should have a diuretic action similar to calcium chloride.

With a knowledge of the work of Haldane and due to the fact that calcium chloride had an irritating reaction, Keith substituted the ammonium chloride salt for the calcium chloride. Keith, Barrier and Whelan [11] 1925, reported satisfactory results with the use of ammonium chloride in the treatment of edema. Gamble, Blackfan and Hamilton [12] 1925, used the sulfate and chloride and also reported favorable results.

Experimental

Desiring to determine the effect of ammonium chloride on the normal individual we studied 39 of the subjects which had previously received sodium bicarbonate. One week following the ingestion of the bicarbonate, when their weight had returned to normal, we collected the following data: (1) pH of the morning urine before administering ammonium chloride, (2) the body weight before ingesting 18 grams of ammonium chloride (12

capsules of 7.5 grains daily for three days), (3) the pH of the urine the morning of the fourth day, and (4) the body weight the morning of the fourth day. The results may be summarized as follows:

Weight Changes in 39 Subjects Receiving Ammonium Chloride

I. *Decreased weight:* 31 subjects lost a total of 61 pounds, the greatest loss being 3.75 pounds and least 0.5 pound.

II. *Increased weight:* 4 subjects gained a total of 4.25 pounds, the greatest gain being 2 pounds and the least 0.5 pound.

III. *No weight change:* 4 subjects showed no weight change.

IV. *pH changes:* The decrease in pH accompanying the administration of ammonium chloride was approximately one half as much as the increase noted with the sodium bicarbonate, the greatest decrease being 1.47 pH. The degree of pH change in the urine did not indicate the degree of weight loss.

Deductions

The Mechanism of Diuresis Produced by Hyperventilation: During hyperventilation two substances leave the blood stream, (1) carbon dioxide and (2) sodium. As early as 1918, Henderson and Haggard [13] observed that the "blowing off" of carbon dioxide produced a reduction of carbon dioxide content of the blood and this soon led to a reduction of the carbon dioxide capacity (alkaline reserve) of the blood. "Apparently alkali passes out of the blood into the tissues." They also noted that when the alveolar carbon dioxide was again raised the "alkaline reserve" was restored, "due apparently to the passage of alkali from the tissues into the blood."

In the light of subsequent work on hyperventilation it becomes evident that the kidney shares with the other body tissues in the passage of the sodium from the blood stream. The percentage increase in sodium phosphate excretion during hyperventilation is always greater than the percentage of water increase, e.g., accompanying a five-fold increase in water excretion there is a six-fold increase in sodium phosphate excretion. This statement is supported by the inclusive data of Collip and Backus [4]; however, they neglected to stress the relation. Leathes' [3] data also show that hyperventilation for 20 minutes may increase the urinary output from 56 c.c. per hour to 123 c.c. and this is accompanied by an approximate three-fold increase in urine alkalinity (36 per cent to 91 per cent). This increase is doubtless due to the increased excretion of alkaline phosphate.

Normally the disodium phosphate does not pass through the kidney due to the fact the sodium salt of such a weak acid dissociates and the free sodium ions combine with the carbon dioxide of the blood stream. During hyperventilation the carbon dioxide of the blood is depleted and allows the sodium to pass as the disodium phosphate, exerting a diuretic action.

The Mechanism of Diuresis Produced by Ammonium Chloride: Since

both calcium chloride and ammonium chloride are effective in treating edema, it is evident that the action of these salts is not due to a specific action of the cation. They are salts of weak bases and strong acids, and therefore in solution yield an acid reaction. The body tissues are normally alkaline in reaction and may be considered as *sodium proteinate,* the negative electric charge on the protein being due to the presence of sodium. Acids such as hydrochloric have a tendency to reverse the charge on the protein, producing *protein chloride.* It is evident that between these two extremes the protein becomes electro-neutral (isoelectric).

At the isoelectric point proteins have, (1) electrical neutrality, therefore, (2) maximum cohesions, therefore, (3) maximum surface tension, therefore, (4) smallest mass possible, and therefore, (5) least hydration capacity. Also proteins at their isoelectric point can combine neither with anions nor cations.[14] It is evident that any agent which brings the body proteins near their isoelectric point would cause the freeing and elimination of (1) sodium and (2) water; apparently calcium chloride and ammonium chloride are such agents.

Mechanism of Water Retention by Sodium Bicarbonate: The chemical nature of sodium bicarbonate is opposite to that of ammonium chloride—sodium bicarbonate being the product of a strong base and weak acid, while ammonium chloride is the product of a weak base and strong acid; therefore, in solution, sodium bicarbonate produces an alkaline reaction and ammonium chloride an acid reaction.

We have furnished evidence that the two salts have an opposite effect on water balance in the normal individual. It is also evident that the two have an opposite effect on the carbon dioxide combining power of the blood —the ammonium chloride producing a lowering,[11] while the sodium bicarbonate produces an increase.

If one desires to increase the solubility (hydration) of fibrinogen, caseinogen, urinary casts, mucus, stearic acid and most organic compounds, he uses alkali, not acid; therefore, the increased hydration of body tissues accompanying the use of sodium bicarbonate is not surprising.

The intensive and extensive studies conducted approximately a quarter century ago still dominate our thought processes. As a result, we still overemphasize the importance of the plasma and desire to explain all respiratory exchange as a function of the plasma bicarbonate. With such a preconceived idea, it appeared logical to assume that deficiency in circulation could be compensated for by increasing the blood bicarbonate. Many have not yet grasped the idea expressed as early as 1920, by Haggard and Henderson[15]: "It thus appears that the corpuscles dominate the plasma so powerfully that the alkali of the (unseparated) plasma at a certain tension of CO_2 is essentially an expression of the alkali-producing power of the corpuscles. The plasma alkali is only a part of the total alkaline reserve of the blood. The chief buffer is the hemoglobin." According to Van Slyke,[16] as much as 85

per cent of the base necessary for the transport of carbon dioxide is obtained directly or indirectly from hemoglobin; and, more recently, Roughton [17] has presented evidence that as much as 20 per cent of the carbon dioxide may be transported by combining directly with the hemoglobin forming carbamino compounds.

Sodium bicarbonate may serve as the first line of defense against acids, but the transport of carbon dioxide is essentially a function of the hemoglobin. It is evident that the blood cells must circulate to perform this function. Hyperventilation does provide better aeration, and better carbon dioxide elimination, decreased alkali reserve, also, diuresis and an alkaline urine; however, there is absolutely no reason to assume that sodium bicarbonate can be substituted for hemoglobin.

The Use and Abuse of Sodium Bicarbonate: Our findings and deductions are in harmony with the unorthodox, but effective treatment of nephritic edema recommended by Lashmet.[18] He has convincingly demonstrated the value of acidosis in the production of diuresis and the elimination of edema in chronic nephritis. The results of his careful studies prompted him to use the following diet in his treatment of nephritis edema—low protein, "salt poor," with a neutral ash. He has added to this, acids or acid-producing salts and "forced" fluid intake. The results of such a regime have proved satisfactory.

Many physicians make a routine practice of prescribing alkalies, and also alkali diet, in the treatment of nephritis. They usually do so with no better reason than "if it does not benefit the patient, it can at least do no harm." Also the general public has been "sold" on the idea that all human ills result from a "too acid" condition, and the panacea is alkali. Berger and Binger [19] have observed impaired renal function accompanying alkalosis, resulting from the alkaline treatment of peptic ulcer. Steele [20] has also observed that renal damage may occur in the alkaline ulcer treatment before clinical symptoms of alkalosis appear. Recently Ziegler and Brice [21] have stated, "The ability of the kidney to excrete solids and to concentrate the urine is greater when the urine is acid than when it is alkaline or neutral." They also warned against the indiscriminate use of alkalies, as alkalization of the urine may defeat the purpose, which is the elimination of solids.

We have no evidence that prolonged use of an acid salt has an injurious effect on the kidney. Very recently Noth [22] has reported the treatment of a case of Pick's disease in which 6 grams of ammonium nitrate were administered daily for over three years with no evidence of hepatic or renal damage.

Conclusions

1. A total of 36 grams of sodium bicarbonate administered over a period of three days was sufficient to cause a weight increase in 90 per cent of the subjects studied; the average weight gain being 2.28 pounds per individual.

2. A total of 18 grams of ammonium chloride administered over a period of three days produced a loss of weight in 80 per cent of the subjects studied; the average weight loss being 1.97 pounds per individual.

3. Ammonium chloride, like hyperventilation, produces diuresis and both produce a decrease in the alkaline reserve as measured by the carbon dioxide combining power of the plasma.

4. The administration of sodium bicarbonate produces an increase in alkaline reserve and an increased hydration of the tissues.

5. The action of sodium bicarbonate in producing increased body hydration is analogous to its action in laboratory procedures.

6. In certain select cases the administration of the alkalies may improve kidney function by dissolving the casts (increase their hydration capacity).

7. The indiscriminate use of alkalies should be discontinued as prolonged alkalization of the urine has an injurious effect.

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THE DEMENTIA PRAECOX PROBLEM *

By G. W. Dishong, M.D., F.A.C.P., *Omaha, Nebraska*

Dementia praecox with its involved interests—social, economic, and clinical—is today the outstanding problem of psychiatry. It is estimated that from 30,000 to 40,000 new cases develop annually in the United States. And, roughly speaking, 25 per cent of the admissions to our state hospitals, and 50 per cent of the chronic cases belong in the dementia praecox grouping. The social and economic implications of the problem are obvious when we consider the nature of dementia praecox. This disorder with its varying degrees of personality distortion accounts for the majority of our social misfits, and involves the expense for their custodial and hospital care. The clinical significance of the problem beggars description and is attested by the enormous amount of investigation still in progress, and the voluminous literature that has been produced.

Introduced about the time when the etiology and interpretation of general paresis were moot questions, dementia praecox was approached from similar angles, and became a subject of widespread interest at home and abroad. The active controversy dates back some 35 or 40 years when the term was popularized by Professor Kraepelin. Throughout subsequent years there has probably been more speculation and clinical interest centering about dementia praecox than any other psychiatric problem. The subject has always been controversial, especially the etiological factors.

Says Professor Kraepelin, "Dementia praecox consists of a series of states, the common characteristic of which is a peculiar destruction of the internal connections of the psychic personality. The effects of this injury predominate in the emotional and volitional spheres of mental life." . . .

"I got the starting point of the line of thought which in 1896 led to dementia praecox being regarded as a distinct disease, on the one hand from the overpowering impression of the states of dementia quite similar to each other which developed from the most varied initial clinical symptoms, on the other hand from the experience connected with the observations of Hecker that these peculiar dementias seemed to stand in near relation to the period of youth. As there was no clinical recognition of it, the first thing to be done for the preliminary marking off of the newly circumscribed territory, was to choose a name which would express both these points of view. The name 'dementia praecox' which had already been used by Morel and later by Pick (1891), seemed to me to answer this purpose sufficiently, until a profounder understanding would provide an appropriate name."

"It has since been found that the assumptions upon which the name chosen rested are at least doubtful. As will have to be explained more in

* Read at the St. Louis meeting of the American College of Physicians, April 23, 1937.

detail later, the possibility cannot in the present state of our knowledge be disputed, that a certain number of cases of dementia praecox attain to complete and permanent recovery, and also the relations to the period of youth do not appear to be without exception. I certainly consider that the facts are not by any means sufficiently cleared up yet in either direction." [1]

Bleuler's theories and his suggestion of the term "schizophrenia" were valuable contributions; he wrote as follows: "As the disease needs not progress as far as dementia and does not always appear *praecociter*, i.e. during puberty or soon after, I prefer the name 'schizophrenia.'"

"This disease may come to a standstill at every stage and many of its symptoms may clear up very much or altogether; but if it progresses, it leads to a dementia of a definite character. . . .

"Latent schizophrenias are very common under all conditions so that the 'disease' schizophrenia has to be a much more extensive term than the pronounced psychosis of the same name. This is important for studies of heredity. At what stage of the anomaly any one should be designated as only a 'schizoid' psychopathic, or as a schizophrenic mentally diseased, can not at all be decided as yet. At all events, the name latent schizophrenia will always make one think of a morbid psychopathic state, in which the schizoid peculiarities are within normal limits. Social uselessness, catatonic symptoms, hallucinations, delusions, make certain the practical diagnosis of the acute mental disease." [2]

Schizophrenia is being used more and more to displace the term dementia praecox. But schizophrenia has been translated to mean "splitting of the mind" or "splitting of the personality," and the terms are used so literally that the meaning is confused.

Many causes have been advanced in the etiology of dementia praecox: heredity, constitutional deficiencies, autointoxication, endocrine disturbance, anatomical lesions, histologic changes in the brain, and troublesome complexes as pointed out by Freud and Jung. All these theories have staunch supporters, and the controversy continues. Both Kraepelin and Bleuler hold to the theory of histologic changes in the brain in the etiology of dementia praecox. Kraepelin states: "The morbid anatomy of dementia praecox does not show macroscopically any striking changes of the cranial contents; only occasional thickening and oedema of the pia are reported, the latter evidently a result of agonal processes. On the other hand, it has been shown that in the cortex we have to do with severe and widespread disease of the nerve tissue." [3]

Bleuler seems less positive in his theories, but he, too, points to structural changes in the brain. He writes: "We do not know as yet on what the pathologic process is based. In acute stages various kinds of changes in the ganglion cells are found. In old cases the brain mass is reduced a little; many ganglion cells, especially in the second and third layer, are changed in various ways; sometimes the fibrils of the cells and the axis-cylinder look

diseased. The findings can not as yet be lined up together nor interpreted as to their causes and effects.[4]

"Then there is presented the theory of Claude—that of separation of dementia praecox as organic from schizophrenia as functional." [5]

Noyes, a recent author, summarizes briefly as follows: "Of the histological work on the brain of schizophrenics some of the most important is that of Dunlap who examined control cases and was unable to find any of the 'dropping out' of cells described by European neuropathologists. He observed many of the histologic changes that have been described in the literature, but found identical ones in the brains of mentally normal persons killed by accident, and therefore concluded that any nerve cell alterations at present described in schizophrenia are due to postmortem changes and other unknown factors, probably some of them technical." [6]

Hereditary factors in the etiology of dementia praecox have received much study. Kraepelin's statistics quote also the results of other investigators, showing hereditary predisposition in from 52 to 90 per cent of the cases. Reports of recent investigators are impressive and indicate the importance of heredity. But we have little information that is definite or convincing. There are many factors involved, and one can not separate the influences of environment and a tainted heredity. Kraepelin aptly remarks: "The causes of dementia praecox are at the present time still wrapped in impenetrable darkness." [7]

There remains a distinguished worker and author, Adolf Meyer, who strikes a more responsive chord when he writes as follows: "Nobody can have absolute guaranty of healthy progeny. All parents need a good dose of preparedness to accept whatever fate may bring in their children. The progress of the world has done much to guide us if we are wise, and, fortunately, on the constructive side as well as on the preventive. Let us not forget that those who may have a tainted stock and some cause for worry may be able to make good and render valuable service to all. Those forewarned are more likely to be thoughtful about the child than those who play ostrich and make it their practical and even religious duty to be blind to the great facts of experience. And when the forewarned improve the chances of their own children, it will be for the good of all." [8]

Meyer also says, "Instead of considering psychiatry a field of asylum diseases, let us see what we find wrong in behaviour and mentation, without damning it at the outset by a terminology derived from merely possible terminal developments. The personality-reactions present themselves to us concretely in terms of reaction-groups; mood disorders, fears, obsessions, states of panic, seclusiveness, fancy states, simple or disorganizing, and memory, retention, judgment and behaviour disorders—plain facts which do not necessitate any very learned or bewildering vocabulary. We look for concrete mismanagement of home situations, for discrepancies of ambition and performance, existing difficulties and failures, problems of adaptation

and problems of desensitization; and doing so, we shall be helpful to our patient instead of sacrificing him at the altar of vocabularies dealing with terminal states and with fixed fatalistic 'constitutions' and too dogmatically fixed 'disease entities.'" [9]

I think we may say that the most important contributions to the present controversy have been the formulations of Dr. Meyer. First expressed more than 25 years ago, Meyer's conception of dementia praecox has stood the test of time. Throughout he has stressed a psychobiologic concept with "total function" in the interpretation of dementia praecox reactions. Meyer favors a dynamic interpretation of the symptoms, and would call dementia praecox an "incidentally organic disease."

Writes Dr. Meyer, "My main assertion has, however, been the fundamental importance of the psychogenic material, and a refusal of hard and fast nosological doctrines. In the *Psych. Bulletin,* 1908, V, 257, I briefly characterized the group as presenting essentially substitutive reactions, the types of defect and deterioration of which show: 'Existence or development of fundamental discrepancies between thought and reaction, defects of interest and affectivity with oddities; dreamy fantastic (crazy), or hysteroid or psychasthenoid reaction, with a feeling of being forced, of peculiar unnatural interference with thought, etc., frequently with paranoid, catatonic, or scattered tantrums or episodes.' I further advocated that it was possible to formulate the main facts of most cases in terms of a natural chain of cause and effect, utilizing the psychobiological material at hand, better than a dogmatic assumption of a specific but hypothetical unitary toxic principle. . . .

"Any psychopathological consideration must today give unbiased consideration to these three aspects: (1) collisions of functions as such, with possible incidental disorders of the organic balance of these functions (hysteria psychasthenia, nervous dyspepsia, and other conflicts of function); (2) the plainly and essentially submental toxic or metabolic illadjustments (alcoholic, metasyphilitic processes, hyper- and hypothyroidism, etc.); (3) the rôle of factors attacking more or less localized mechanisms of neurological balance, such as the hypothetical frontal lobe mechanisms of Kleist (symptom-complexes produced by focal lesions, tumors, etc.).

"Pathology of today must work with all these types of integration without favoritism, and show just how far any one of the individual components can do justice to the explanation of any experiment of nature. . . .

"Let us not forget that the preëminently psychogenic conception of dementia praecox formulates the clinical problem so that in some cases at least dangerous constellations can be pointed out in time. At the same time it formulates problems of investigations, and would not seem to be as likely to block necessary investigations as the exclusive faith in merely hypothetical poisons and as yet unexplained, but after all most probably incidental lesions, wholly sacrificing the fruitful field of psychobiology." [10]

It is not generally understood that psychiatry has undergone extraordinary changes since the turn of the present century. The majority of physicians whose training dates back 30 or 35 years are frank to admit that in their student days psychiatry seemed mystical and a thing apart from general practice. Today a recent graduate has fairly good understanding of the mental processes in all forms of human behavior, and recognizes psychiatry as an important and integral part of general medicine. The old psychiatry was largely static and descriptive, the new is dynamic and analytic. This change has not been sudden or revolutionary, but rather in the nature of a development which is still in progress. And the transitional period bridging the old and new psychiatry is recorded in a literature that has added greatly to the sum of our psychiatric knowledge.

We may mention two important events that had much to do with this change in psychiatric thought—the dementia praecox controversy and the analytic psychology of Freud and his followers. If the student will familiarize himself with the development of the dementia praecox concept in all its phases, he will have access to a fund of psychiatric knowledge that encompasses the entire domain of mental disorders.

But just as dementia praecox is still controversial, so is there still misconception about the technic and application of psychoanalysis. However, all psychiatrists are using mental analysis in some form. And while prolonged and detailed psychoanalysis is rarely necessary, there seems no question that Freud's theories are scientifically sound. To be sure Freud's psychology has shocked our smug complacency at times, it has confused our moral values, and has well nigh rendered obsolete such terms as "normal" and "abnormal" in relation to human conduct. But there seems no question that the analytic psychology of Freud and the Zurich school has given us far better insight into all forms of mental activity, and vastly improved psychotherapeutic measures. As far back as 1917 Putnam declared, "Who would have dreamed a decade or more ago that the college professors would be teaching Freud's doctrines to students of both sexes, scientific men turning to them for light on the nature of the instincts, and educators for hints on the training of the young?" [11]

There are those who declare that psychiatry has made more progress in the present century than in all previous time. This statement seems rash and it is misleading. Psychiatry has been a development; its aim and scope are broad, and to be in truth "the science of human behavior" psychiatry must touch human adjustment at many points; but to do this psychiatry is dependent upon other sciences, such as biology, physiology, sociology, and psychology. I think we are justified in expecting far greater development in the next generation than has occurred in the past. But psychiatry as we now know it is far from being an exact science, and there is much to be done for psychiatry and to psychiatry. Until psychology affords a more rational explanation of such phenomena as consciousness, sleep, memory

and sense-falsification, we shall continue to deal in abstractions and metaphysical formulations—relics of the old descriptive psychiatry. For the present the aim of psychiatry must be along the lines of mental hygiene and prevention. That is to say, psychiatry affords relief in many situations, and achieves remarkable success in certain selected cases; but the strictly therapeutic possibilities in the practice of psychiatry compare very unfavorably with the results obtained in internal medicine and surgery. There is a large and steadily increasing number of people who fail to make harmonious adjustment to the ordinary stresses of life, and suffer varying degrees of mental unrest and disability. In this great group we find the psychoses and psychoneuroses, only a small percentage of which find permanent relief in psychotherapy, notwithstanding the designation "functional" mental disorders. This is a definite challenge to psychiatry.

Throughout its history the treatment of dementia praecox has been confused and unsatisfactory; and there are few recoveries after the definite psychotic breakdown. Numerous and varied therapeutic methods have been acclaimed only to be abandoned or used occasionally in selected cases. But here again the student will be richly rewarded by a careful review of the therapeutic procedures and their results. Endocrine therapy was enthusiastically investigated at an early period, and is still being tried; fever therapy in its various forms has been in vogue for years, and is again being stressed; inhalations of oxygen and carbon dioxide; prolonged sleep induced by various sedatives, and more especially sodium amytal; the use of normal blood, convalescent serum, insulin, and other forms of biologic treatment. These and many other forms of therapy have been tried and found wanting. However, recent reports on insulin treatment are more encouraging; some authors claim as high as 70 per cent recoveries in new cases, and less favorable results in old cases.

Psychoanalysis has proved beneficial in a small per cent of cases treated in the pre-psychotic stage. But this procedure is not advisable after the psychosis is established. It is in the early or pre-psychotic stage that mental analysis and reëducation would seem indicated. If one studies the schizoid tendencies that finally culminate in schizophrenic disease, it is not difficult to trace the beginnings to psychic peculiarities and conditioning influences in the formative period of life. While treatment of the psychosis appears discouraging, the situation is not as hopeless as it would seem. If we follow the genetic-dynamic interpretation of Dr. Meyer, and accept the psychobiologic concept of personality, it is at once apparent that each case is a law unto itself, and that no two cases can be treated alike. There is always some conflict or overload to account for the final break, and the individual should be treated accordingly.

Routine treatment in vogue at the present time may be summarized under four headings: hydrotherapy, occupational therapy, recreational therapy, and reëducation; the aim is to direct the patient's interests and activities

into useful channels. These procedures usually result in improvement if carried on in the shelter of an institution. But too often such improvement is only temporary, the maladjustment and nervous symptoms recurring when difficult situations are again encountered. The seclusion of the hospital treatment favors repression of the intrapsychic conflict; actual improvement requires understanding of the conflict and its sublimation. "The methods that reveal the causes may properly be called psychoanalytic, while the methods by which the causes are corrected are primarily a matter of the re-education of the emotional and volitional life at the sources of motivations." [12]

Psychiatry is centering more and more in the consideration of personality traits and tendencies. But personality has come to mean far more than temperament or mentation. "The personality," says Dr. Campbell, "is not something outside of and apart from the constituent organs of the body; it is the total activity of these organs more adequately conceived. The study of the personality and its disorders involves the study of all the bodily organs, but in a more complete setting than is necessary in internal medicine. . . .

"The personality, in the face of difficulties, may find refuge in phantasies, deliria, or hallucinations, but also in aches and pains, and palsies, and the latter may be as truly evidence of mental disorder as the former." [13]

The great central fact of human adjustment is conflict. Man's natural endowments are those of a primitive, while modern civilization demands highly socialized adjustments. At best the personality is forced, and a certain amount of conscious suppression and unconscious repression are necessary before the individual can become a socially adjusted member of his community. If there is emotional warping, intellectual defect, endocrine disturbance, or structural alteration, there will be relative handicap and conduct will suffer accordingly. But in spite of obstacles life must carry on.

It has long been argued that the mental impairment accompanying schizophrenia is not true dementia, and that the term dementia praecox is a misnomer. In organic brain disease, with structural changes leading to actual dementia, there is rather general reduction in mental capacity; whereas in dementia praecox the emotional life is often seriously disordered, while orientation and memory are only slightly impaired. Such patients may exhibit sudden anger and violence without apparent provocation; giggle and express pleasure, when the opposite mood is expected; interest is lacking, attention and concentration suffer, and the emotional responses generally are not in keeping with the situation. This is not a true dementia, and this characteristic has been called emotional or affective deterioration.

Study of the emotions and instinctive drives, with their effect on interest, sentiment and judgment, has been a great aid to students of human nature. From these studies has come a better conception of individual psychology and the realization that human behavior is determined more by unconscious

dynamic trends than by conscious deliberation. And, finally, there has evolved the theory of libido or interest as the basic common denominator to be used in the appraisal of human adjustment. But libido as here used implies not only the instinctive reactions; it implies all our desires, hopes, and ambitions.

In health the libido or interest flows outward to the environment, and is occupied with socialized adjustments. This "socialization of libido" implies that social ends be served rather than personal ones. In dementia praecox the libido is withdrawn from the environment and turned inward through a process of introversion to be utilized in phantasy. Here the unconscious primitive and infantile complexes are absorbing the libido, and in extreme cases the libido is occupied entirely with fantastic thinking and symbolic gratification. This accounts for the strange and apparently meaningless conduct of the schizophrenic, and it is for this reason that some authors have designated the schizophrenic mechanisms as "unpsychologic." When we compare the libido strivings of dementia praecox and the psychoneuroses we do find similarity, especially in the pre-psychotic stage of dementia praecox. But after the psychosis is established the disturbance in affect is apparent and characteristic. According to Ferenczi, "The neurotic gets rid of the affects that have become disagreeable to him by means of the different forms of displacement (conversion, transference, substitution); the patient suffering from dementia praecox, on the other hand, detaches his interest from objects and retracts it to his ego (autoerotism, grandiose delusions)." [14]

Mind has always been elusive and difficult to understand. Throughout the ages the mind of thinking man has tried to explain the mysteries of life and living. Mythology, philosophy, and religion, have all been the expression of man's spiritual strivings—the quest of the soul for its infinite origin. This projection or reaching out of man's interest has been the means of human progress; it led to imagination, constructive thinking, new concepts and invention. And the race history of this development and evolution has been preserved in a philogeny that is relived in the life span of the individual. The libido theory implies a dynamic psychology with psychic energy under pressure; and the direction taken by this energy flow determines the health and usefulness of the individual. If for any reason the energy is dammed up or no longer flows outward in self-expression, it then flows backward, using again the channels that were active in primitive or infantile life. Hence we may say that in schizophrenia we are dealing with a personal "substitutive reaction," and not a disease entity.

To understand life a person must have knowledge of himself and knowledge of the world in which he lives. To accept the facts of life without evasion and be able to meet the challenge with courage and zest —that is successful living. The schizophrenic fails because of his intrapsychic disharmony. His mind is not acting in concert—thinking, feeling

and acting are not blended into reaction appropriate for the occasion. Stress and conflict have resulted in overload and exhaustion, and finally when confronted with some difficult, though not uncommon, situation the " splitting " process is complete, and the personality is said to have disintegrated.

The dementia praecox problem is a definite challenge to psychiatry. As I see it the concept is too broad and the formulations concerning etiology, symptomatology, and treatment are vague and unreliable. The disorder begins in youth, and many of the chronic cases live to old age. A very great number are afflicted in mild degree and realize their limitation; these, while definitely incapacitated, do not require hospitalization and try to carry on. In our midst are thousands of these unfortunates who struggle along against a handicap that is most disheartening. Among the milder cases with partial insight suicide is not uncommon. There is tragedy here, stark and unrelenting. But until more light is thrown on the problem our efforts must be largely palliative and along the lines of prevention and reëducation.

But we can say with Dr. Van Rentergren, " Thus the psychotherapeutic as a moral leader fills the roll of guide (*directeur d'ames*), one who helps along the doubter, encourages the toilers, calms the frightened, arouses courage, keeps up hope, and comforts where comfort is needed." [15]

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THE RHEUMATIC ERYTHEMAS; A CRITICAL SURVEY *

By HARRY KEIL, M.D., *New York, N. Y.*

IN several recent publications [1, 2, 3] preliminary data have been incorporated, indicating that there is need to reclassify "the erythema group of skin diseases." In the past there have been included under one broad category, usually termed "rheumatic," a variety of conditions having in common the following features: fever, joint pains, various types of cutaneous lesions, cardiac murmurs of functional or of organic origin, and even prodromal sore throat. Clinico-pathological studies appear to show that this vast *caput mortum* comprises at least six well-circumscribed entities: (1) the rheumatic erythemas; (2) erythema multiforme exsudativum (Hebra); (3) Osler's erythema group (capillary toxicosis of Frank); (4) acute "systemic" lupus erythematosus, by some termed chronic erythema multiforme; (5) gonococcal erythema multiforme; (6) meningococcal erythema multiforme. It seems desirable to differentiate the various types, as such distinctions may aid in the formulation of rational methods of treatment and the framing of a reasonably accurate prognosis.

In this paper it will be my principal purpose to segregate what may be termed the genuine rheumatic erythemas and their variants. Hitherto, this subject has been the concern of pediatricians [4, 5] or of internists,[6] but it seems desirable to add observations based on a correlation of the dermatological and internal medical manifestations. In order to point out some of the many problems arising in connection with these cutaneous lesions, illustrative case protocols will be appended at the end of the article, together with brief comments regarding diagnostic points. In this manner, also, an opportunity will be afforded to point out the importance of heart disease as an essential feature of this group of cases.[16]

INTRODUCTORY HISTORICAL DATA

Rayer (1835) has been credited by some writers with the first description of erythema multiforme as observed in rheumatic fever,[7] but perusal of original sources reveals that this investigator considered articular pains as the ultimate criterion of the rheumatic affection. Long before this, Wells [8] and then Bright [9] had recorded the occurrence of erythemas in undoubted examples of rheumatic fever, but they were unaware of the significance of these rashes. In the middle of the nineteenth century the conception of "arthritism" was in vogue, only to be replaced by the equally vague one of "rheumatism." Although an attempt was made to study dermatoses in terms of systemic disease, little success was achieved in this

* Received for publication October 20, 1937.

direction owing to the use of vague and even erroneous criteria. In the course of time, therefore, a heterogeneous group of conditions was assembled under the head of erythema multiforme (polymorphous erythemas).[10] For example, Lewin,[11] gathering cases of "erythema multiforme exsudativum," stressed the systemic features and included endocarditis as one of the associated findings. His conclusions, however, lose in validity, as he made no attempt to distinguish the different clinical pictures embraced by this generic name. Lewin's statistical compilation is of fundamental interest, for it has been repeatedly cited in modern works; it will be referred to again. Concrete description of the rheumatic erythemas appears to have been made first by Barlow and Warner (1881)[12] who recorded the association of erythema marginatum rheumaticum with subcutaneous nodules, and dissemination of this knowledge was promoted largely through the outstanding works of Cheadle [13] and of Garrod.[14] It seems that better understanding of the clinical importance of these eruptions had to await crystallization of a more accurate clinical conception of rheumatic fever.

Criteria for the Diagnosis of a Rheumatic Eruption

In studying the manifestations of rheumatic fever, it seems essential to establish precise limits in the definition of this disease; otherwise, confusing elements are apt to be introduced. The status of many dermatoses, formerly attributed to this condition, appears to be subject to reconsideration, for such relationship was adduced on the basis of criteria of doubtful nature. An eruption may be considered as of rheumatic origin if the following postulates are satisfied: first, it must be shown (a) that the patient is afflicted with rheumatic fever; and (b) that the disease is active. Relative to the latter criterion, there are certain exceptions which will be mentioned in subsequent sections. Second, the rash must be related to the rheumatic affection in such manner as to exclude, with reasonable certainty, the possibility of coincidence of conditions.

(*1a*): The clinical observations reported in this paper are based on a study of the records of 523 cases of rheumatic fever admitted to The Mount Sinai Hospital during a period of about five years. A substantial proportion of the patients had been previously followed over intervals ranging from one to ten years or longer, and in 20 per cent of the cases the diagnosis was verified post mortem. In the remaining instances the clinical evidence required for the recognition of this disease was definitely established. The criteria followed closely those described in the comprehensive volume issued by the Heart Committee of the New York Tuberculosis and Health Association,[15] except that, for the purposes of this study, it was deemed essential to insist on definite evidence of heart disease, in one form or another, as the chief feature of this condition.[16] It was realized that in some instances substantiating clinical evidence might be lacking for the time being; when, however, postmortem data were available, cardiac in-

volvement was considered obligatory for diagnosis. It was found that by the strict application of this principle, the various members of "the erythema group" seemed to fall into natural and orderly categories.[17] Doubtful instances and those classified as "rheumatic" only after much controversy were intentionally excluded. There were also eliminated those cases featured by the engrafting of another condition on rheumatic heart disease, for example, acute and subacute bacterial endocarditis.

(*1b*): The division of the material into active and inactive rheumatic heart disease was considered as essential in evaluating the clinical significance of the rashes. The fact that an eruption is encountered in a patient afflicted with rheumatic fever does not necessarily imply a relation between the two conditions. At first, for the particular purposes of this study, it was felt best to include only those cases featured by evidence of activity in the rheumatic process (progressive heart involvement, joint manifestations, chorea, subcutaneous nodules, fever, rapid pulse [especially at night], leukocytosis, progressive anemia, inability to gain weight [particularly in children], fatiguability, epistaxis, pallor, rapid sedimentation rate, and electrocardiographic changes, etc.). In the average case it was relatively simple to determine the presence of active disease; however, it was more difficult to distinguish between a true exacerbation occurring during intervals of "cure" and an acute attack representing increased intensity of symptoms in a continued low-grade chronic process. There were occasional instances where the aforementioned signs and symptoms were lacking for the time being, and in such cases the final opinion relative to activity rested on the clinical acumen of the observer. It was soon found, also, that in a few patients cutaneous lesions first appeared at the inception or the apparent subsidence of an attack of rheumatic fever, and in such instances observation taught that the eruption per se afforded evidence of continuing or progressive rheumatic disease.

(*2*): A dermatosis observed in a patient with rheumatic fever may be coincidental in at least two senses: (a) it may be entirely unrelated, for example, a drug rash; (b) it may be attributed more properly to the sequelae or complications of rheumatic heart disease, such as auricular fibrillation and its secondary effects, cardiac failure, etc.

Incidence of the Rheumatic Erythemas

The incidence of the rheumatic erythemas has been variously estimated (4 per cent to over 62.5 per cent). The general impression, however, is that these dermatoses are rare. West [18] stated that with more accurate diagnosis, the incidence of the rheumatic rashes diminished practically to the vanishing point. Cockayne,[19] criticizing this statement, observed that West had been chiefly concerned with the disease as seen in adults. Leichtentritt [20] collected 10 instances of rheumatic erythemas in children (62.5 per cent of his series of cases); however, this unusually high incidence cannot

be considered as representative, for the figure was arrived at on the basis of small numbers. Coburn [21] recorded 28 examples of erythema marginatum rheumaticum (17 per cent) and Wallgren,[5] discussing the annular variety, reported it in 12 per cent of 146 rheumatic children. Some observers have noted an even higher incidence of these rashes than of subcutaneous nodules during a corresponding period.[4, 22] Though the dermatosis and its variants are most often encountered in childhood, it would seem that the discordance in statistics is only partly explained by the difference in the type of material observed.

Of the 523 cases of rheumatic disease constituting the basis of this study, there were 53 examples of erythemas (10 per cent) regarded as having fulfilled the strict criteria already mentioned; the majority of these rashes was seen by me, so that the descriptions to follow are first-hand. The greatest number of cases occurred in children up to the age of 15 years; the remainder were restricted to young adults, except for occasional instances in older persons. The uncommon occurrence of the dermatosis in infancy can be correlated with the rarity of rheumatic fever during this age-period. The appended table 1 furnishes data on the type of material that was available for analysis:

TABLE I

A. Rheumatic heart disease (no accompanying cutaneous lesions)

	Number	Active	Inactive	Deaths	Postmortems
Children	103	98	5	27	18
Adults	257	196	61	61	47
	360	294	66	88	65

B. Rheumatic heart disease (with various cutaneous lesions as classified in table 2)

Children	79	78	1	20	15
Adults	84	62	22	23	20
	163	140	23	43	35
Total	523	434	89	131	100

Total number of cases ..... 523, of which about 20 per cent verified post mortem
Number of children ..... 182 or 35 per cent of the material
Number of adults ..... 341 or 65 per cent of the material

The majority of dermatoses, including the rheumatic erythemas, was observed in patients in the first and second decades of life. As the dividing line between children and adults was arbitrarily fixed at 15 years, the latter group embraced a substantial proportion of adolescents, thereby increasing the incidence of eruptions in that category. Perusal of table 1 shows that practically all the children were in the active phase at the time of observation; on the other hand, a considerable proportion of adults, chiefly in the older

age-groups, suffered from the effects of inactive rheumatic heart disease or its sequelae. To some extent this explains the difference in the incidence of rheumatic dermatoses as well as of the types of cutaneous lesions encountered.[17]

Altogether there were observed 181 eruptions distributed among 163 patients. The various types of cutaneous lesions are classified in table 2.

Included among these were certain dermatoses which are relatively less important (telangiectasia), or the rheumatic nature of which is questionable (erythema nodosum), or the origin of which is not definitely attributable to activity in the rheumatic process (a part of the purpuras). Even after eliminating these doubtful eruptions, there still remained a considerable number of true rheumatic rashes, this applying notably in the case of the erythemas. The unusually high incidence, especially if considered in relation to the group of children alone (about 25 per cent), can be partly explained by the care exercised in selecting cases for admission and by the

TABLE II

	Cases
Rheumatic erythemas	53
Hemorrhagic eruptions (of various types)	53
Subcutaneous nodules	36
Telangiectasis	11
Scarlatiniform eruptions	8
True urticaria	7
Erythema nodosum	5
Sweat eruptions	5
Herpes zoster	3
Total number of eruptions	181, distributed among 163 patients.

opportunities afforded to follow patients on several or many occasions. This was partially offset by the inability to observe patients throughout the entire clinical course and by the transiency and circumscribed character of certain rheumatic dermatoses, especially the erythemas, which allowed them to be easily overlooked. Some of the discordance in the figures recorded in the literature may be attributed to the labeling of rheumatic erythemas as drug rashes, toxic erythemas of unknown origin, or as unclassified eruptions. The point to be stressed is that any statistical compilation has restricted value apart from a thorough analysis of the individual dermatoses in relation to the rheumatic process.

CLASSIFICATION OF THE RHEUMATIC ERYTHEMAS (RHEUMATIC ERYTHEMA MULTIFORME)

The erythemas observed in rheumatic fever comprised several varieties which could be conveniently classified as follows:

1. Simple papular form
2. Ringed forms: (*a*) erythema marginatum rheumaticum
   (*b*) flat annular erythema

Though there are gradual transitions between various members of this group, each of these eruptions will be considered individually and the evidence for their rheumatic nature discussed under separate headings.

1. *Erythema Papulatum Rheumaticum:* Fourteen instances of this dermatosis were observed. The eruption usually appeared in the form of discrete, dull red papules, match-head to split-pea in size, situated mainly but not exclusively about the articulations. Sites of predilection were the areas about the elbows, knees, arms, and buttocks. The extensor aspects were favored though occasionally the flexor surfaces were chiefly affected. At times the trunk was also involved. As a rule, the rash was composed of a small to moderate number of lesions, disposed bilaterally and symmetrically, but sometimes the dermatosis was confined to one side. The lesions were characterized by transiency, undergoing involution within a few hours to several days (case 1). The tendency to appear in recurrent crops was a striking feature in many patients. Though pruritus was sometimes noted, it was not usually intense. In general, subjective complaints referable to the eruption were absent. Residual pigmentation,[19] found in the other types of rheumatic erythemas, was not observed by me in lesions that were strictly papular.

In several instances the individual papular lesions assumed an urticarial character owing to the occurrence of marked exudation of fluid. This was sufficiently pronounced to warrant the use of the morphologic designation of erythema urticatum rheumaticum, a name which merely emphasizes the clinical importance of this attribute (case 2). Such lesions, often found on the buttocks, may be moderately pruritic.

In several examples under my observation, the dermatosis closely resembled erythema nodosum, owing to the appearance of somewhat nodular tender lesions situated on the lower extremities. It has been pointed out in another publication that many other eruptions acquire these attributes, probably as a result of a superimposed local circulatory factor peculiar to the lower limbs, and that great care must be exercised in differentiating such lesions from banal erythema nodosum. This substantiates the descriptions of a similar phenomenon recorded by Garrod [14] and by Josias [23] in cases of erythema papulatum rheumaticum.

In occasional instances erythema papulatum may be associated with erythematous macules arranged discretely or in patches. The latter represent an abortive attempt at papule formation or constitute a stage in the involution of raised lesions. Simple papular efflorescences may also be seen in association with typical erythema marginatum rheumaticum, as in several patients under my observation (case 3). Among others, Sevestre [24] reported an instance in which erythema marginatum was succeeded by a crop of erythema papulatum. This case is of interest as examination of the heart at first revealed no abnormalities, though polyarthralgias were present early in the course. Subsequently, endocardial and pericardial murmurs became

audible, and graphic studies confirmed the clinical impression of aortic insufficiency. Garrod described a case of erythema papulatum in a child 15 years of age, the eruption being accompanied by trifling articular pains and cardiac murmurs; subsequently, there were many crops of papular and interspersed marginated lesions, accompanied by signs of pericarditis and succeeded by sore throat and numerous subcutaneous nodules. In still another patient Garrod observed the combination of chorea, joint symptoms, endocarditis, erythema papulatum, and erythema marginatum.

Corresponding to the general experience of many observers, the dermatosis was encountered chiefly in children and young adults, with but one exception, a patient 37 years of age (case 4). Occasional examples of this type of eruption occurring in adults suffering from rheumatic fever have also been described by other writers.[25]

It will be seen, then, that in pure form this dermatosis presents few distinguishing features. The most important attributes are the transiency of lesions, recurrences in crops, and the localized distribution of the eruption in many cases. Erythema papulatum rheumaticum is commonly diagnosed as a drug rash and, since sodium salicylate is used most often in rheumatic fever, it is frequently designated as a salicylate eruption. As a rule, these dermatoses can be differentiated from one another. In cases under my observation the rheumatic cutaneous lesions often appeared before institution of salicylate therapy, at times underwent spontaneous involution during the administration of the drug, and could not be reproduced by resumption of medication, even after prolonged use in adequate dosage. In one instance the dermatosis faded rapidly after sodium salicylate was stopped, but this could not be regarded as proof of cause and effect, for rheumatic lesions are characterized by their transiency. On the other hand, salicylate rashes of the papular variety were usually marked by their bright red color, were rarely localized in distribution, showed greater tendency to coalescence of patches over large areas, involved the extensor aspects of the limbs more diffusely, and, when generalized in extent, also affected the face and trunk. Moreover, itching was generally a more pronounced feature. Usually the eruption remained visible several days, and in its involution was often accompanied by some degree of desquamation. In occasional instances, however, the differentiation proved most difficult, if not impossible, and additional observation was essential before a more accurate opinion could be formulated.

Relation to Active Rheumatic Disease

In all 14 cases of erythema papulatum rheumaticum the criteria for the diagnosis of rheumatic fever were fulfilled. In some instances this opinion was not accepted at first, but the nature of the subsequent course dispelled any doubt regarding the validity of this classification. In a few instances the eruption was accompanied by articular pains, usually generalized; no constant association of these phenomena was observed, as the dermatosis

was most often encountered in young persons in whom joint symptoms are not infrequently trivial or absent. In general, the lesions appeared during an acute exacerbation of rheumatic fever, but at times there were no obvious signs of activity in the rheumatic process. In the latter case it was fair to assume that the eruption per se constituted evidence of active disease, an opinion which was corroborated in most patients by the later occurrence of a frank recrudescence of rheumatic fever. No deaths occurred in this small group of cases, nor were any instances encountered where the clinical course could be characterized as unusually severe. It is noteworthy that the examples of erythema papulatum rheumaticum reported in the literature were also featured by relative mildness of course, despite signs of cardiac involvement in practically all such patients. In view of the paucity of observations, no definite conclusions relative to prognosis can be drawn, though the evidence on this point seems suggestive.

2. *Erythema Marginatum Rheumaticum:* Of all the rheumatic erythemas, the marginated type presents the most characteristic morphology. Although scattered descriptions of it are extant in the older literature, concrete evidence of its rheumatic nature was first given by Barlow and Warner (1881)[12] who recorded its occurrence in 7 out of 27 cases of rheumatic subcutaneous nodules seen in children and young adults. In 1890 Garrod [14] offered statistics based on 20 instances of erythema marginatum observed in children. Half of these had suffered from acute articular rheumatism and in seven children there were definite signs of cardiac disease. Of the remainder two had had chorea, three subcutaneous nodules, and five articular pains or a family history of acute rheumatism. Garrod regarded this dermatosis as "conspicuous among the manifestations of rheumatism in childhood." Moreover, he stated that a majority of rheumatic children developed these lesions at some period of the disease, but that the eruption was frequently not recognized, notably when limited to but a few patches. Among the signs and symptoms overlooked by practitioners, Broadbent [26] stressed erythema marginatum rheumaticum, emphasizing its transient course. On the other hand, Findlay [27] in an outstanding study of 701 cases of rheumatic fever in childhood, noted only four instances of the dermatosis; this represents a lower incidence than has been reported by other observers.

Of the 53 rheumatic erythemas recorded in this paper, 15 were examples of erythema marginatum rheumaticum. The dermatosis appeared in the form of numerous circles or segments of circles of varying sizes, occasionally attaining a diameter of several inches. The borders were raised above the level of surrounding skin, were colored dull red, and were sharply circumscribed; individual papules could not be distinguished in the rampart. The contrasting centers were flat and characteristically colored varying shades of brown, sometimes a more livid hue. When isolated patches developed more rapidly than usual, the central areas revealed but little discoloration, though this occurrence was relatively uncommon. By peripheral

extension and coalescence of contiguous rings, polycyclic and geographical figures were produced, resulting in a most bizarre appearance (case 5). In typical instances the lesions were restricted to the trunk, but occasionally spread to the extremities, principally to the upper parts. The mucous membranes appeared to be spared. I have not observed involvement of the face or of the dorsa of the hands and feet, except in one unusual example (case 5). Mackenzie [28] also recorded an instance of rheumatic fever in a child who showed facial lesions in addition to those located on the trunk and limbs; the patient died and postmortem examination disclosed acute rheumatic valvulitis.

The eruption was characterized, further, by sudden onset, rapid spread, and transiency of lesions. In several instances the dermatosis appeared overnight and faded in several hours. Garrod pointed out that such eruptions may occur and disappear in the interim between visits to the hospital. The tendency to rapid changes in morphology of individual lesions and the appearance of successive ephemeral crops are attributes resembling the ordinary clinical course of rheumatic fever itself. Leichtentritt stated that in his group of cases two to three crops occurred on the average during the period of hospitalization, and in one instance as many as eight recurrences were recorded over an interval of 16 weeks. However, this attribute is not exceptional and it has been stressed by many observers. Of 28 examples of erythema marginatum recorded by Coburn,[21] four were persistent over a number of years, with daily fluctuations in intensity. Swift [29] also encountered eruptions lasting for long periods, but it is probable that their longevity resulted chiefly from a succession of crops.

Aside from a temporary dirty-brown discoloration of skin marking previous sites of lesions, sequelae have not been observed. As a rule, scaling is absent. Slight itching and burning have been occasional complaints, but I have not encountered any instance where subjective discomfort was pronounced. Indeed, the dermatosis is often overlooked owing to the absence of subjective symptoms, particularly when there are but few lesions.

Discrete papules are occasionally found interspersed among lesions of the marginated type, suggesting the possibility that peripheral extension of individual papules gives rise to ringed formations. This phenomenon has its counterpart in many cutaneous processes; it is, however, more difficult to establish the occurrence of this sequence of events in cases of rheumatic erythema marginatum, as the lesions have an exceedingly rapid course. The configuration of patches may completely change in astonishing fashion within a few hours and even under direct vision (personal observation).

At times the borders of lesions may become "urticarial," owing to exudation of serum in large amounts; the ramparts may have a whitish glistening appearance, intensified by rendering the surrounding parts taut. Such eruptions may be moderately pruritic at the onset. The resemblances to true urticaria may be heightened by the location and transiency of lesions,

but morphology, clinical course, and lack of pronounced itching in most instances generally aid in differentiating these dermatoses (cases 5 and 6). It may be mentioned, in passing, that ordinary urticaria may occasionally be caused by rheumatic fever; nevertheless, it seems advisable to distinguish "urticarial" eruptions from genuine hives, though in some cases this distinction may be difficult to establish.

On the other hand, the peripheries of lesions may be but slightly papular, forming a transition to the flat annular variety described by Lehndorff and Leiner. On several occasions I have observed flattening of the borders of erythema marginatum rheumaticum, so that just before complete involution the appearance of the macular type was simulated. In many instances the precise classification of the dermatosis will depend on the features exhibited at the time of observation, and in all likelihood the number of cases included under the category of erythema marginatum rheumaticum represents an inaccurate estimate of its incidence. This is, however, of no great moment, as clinical evidence shows the close alliance of these varieties of rheumatic eruptions.

Included in the group of erythema marginatum rheumaticum were several examples of gyrate and serpiginous dermatoses, the essential features of which were similar to those exhibited by the former type, except that the advancing borders were usually less raised and the characteristic central brownish zone of discoloration less conspicuous (case 7). Gyrate, serpiginous, and marginated lesions may be observed occasionally in the same patient, either in the same attack of the disease or in subsequent exacerbations (cases 8 and 9).

In one instance (case 10) the mother of the patient described the antecedent occurrence of transient "ringworm," the lesions having been situated on the upper limbs. As far back as 1890 Garrod [14] remarked that mothers often mistook erythema marginatum rheumaticum for ringworm (tinea circinata), and he emphasized the point that a history of "ringworm" appearing on the limbs and characterized by *rapid spontaneous involution*, should direct attention to the possibility of rheumatic origin. Isolated lesions of erythema marginatum rheumaticum, though occasionally resembling tinea circinata, differ in the absence of a vesicular border and in their rapid disappearance without local treatment.

Erythema marginatum rheumaticum is most often encountered in children, but occasional examples have been observed in adults. In the series of cases recorded in this paper, the eruption was practically always seen in children whose ages ranged from between 3 and 15 years; only two instances were observed in adults, both patients being 26 years of age (case 11).

Before considering in detail the evidence for the rheumatic nature of this dermatosis, it may be pertinent to conclude this section with a brief description of an unusual example of rheumatic fever (?) manifesting atypical cutaneous lesions, the appearance of which was similar to, but not identical

with, ordinary erythema marginatum rheumaticum. This case was not included in the statistics.

The patient, 16 years of age, had been afflicted with rheumatic heart disease for many years. On examination physical signs of mitral stenosis were noted. The voided urine was colored dark-brown, gave an intense guaiac reaction, contained albumin, and its sediment showed two to three red blood cells per high power field. In addition, the spleen became palpable subsequently, so that the possibility of subacute bacterial endocarditis was considered; however, cultures of blood were repeatedly sterile. There was no evidence of diminution in cardiac reserve. During the course no additional valvular defects were found. The temperature curve was extraordinary. It was remittent in type with elevations to 105° F. or 106° F. every fifth or sixth day. On several occasions the precipitous rise in temperature was accompanied by unusual cutaneous manifestations that differed in appearance from time to time. On one occasion there were numerous erythematopapular lesions showing reddish brown borders and relatively depressed purplish blue central areas. Many efflorescences were oval in shape, simulating the appearance of pityriasis rosea. The size ranged from 0.5 to 1.5 cm. in their longest diameter. The eruption was situated chiefly on the limbs and, to a lesser extent, on the trunk. A striking feature was the occurrence of lesions on the forehead, lower aspects of the face, and near the margins of the limbs. Some of them were slightly tender when pressure was applied. The eruption faded by the following day. On another occasion there appeared flat rings of erythema about the size of a quarter piece, the centers of which were colored pale blue; the lesions were located on the chest, arms, thighs, back, and cheeks. At this time the temperature had risen to 105.4° F. and the patient complained of pain in the right hip. The rash underwent complete involution within 24 hours. Six days later the temperature again soared to 105° F. and there appeared on the thighs symmetrical rings of erythema within other rings, producing an iris-like (rainbow) configuration. The largest diameter of the lesions was about that of a silver half-dollar piece. In its manner of origin, location, absence of vesiculation, and rapidity of involution (several hours), the eruption seemed to differ from erythema multiforme exsudativum (Hebra); the differential features of the latter condition will be considered in greater detail in a succeeding section.

On examination, several months later, the patient showed the physical signs of mitral stenosis, mitral insufficiency, aortic insufficiency, and, for the first time in this extended period of observation, auricular fibrillation. It is probable that the case was one of rheumatic fever, though many features seemed to point in the direction of subacute bacterial endocarditis.

Relation to Active Rheumatic Disease

The evidence for the rheumatic nature of erythema marginatum is chiefly clinical. In many instances it appears at the height of rheumatic activity or during some phase of active disease. This rule seems to be substantiated by my observations, though certain qualifications must be introduced.

Barlow and Warner [12] recorded seven instances of erythema marginatum encountered in 27 patients manifesting subcutaneous nodules; these cases concerned children and young adults. I have observed at least four examples illustrating this combination of features; three of these have been cited in the case protocols (cases 5, 6, and 9). In children, particularly, this eruption may be the "revealing symptom" of rheumatic fever. Occa-

sionally it may be combined with chorea as the initial manifestations of an incipient attack of the disease. Coburn described an instance in which erythema marginatum, tonsillitis, and chorea appeared long before the subcutaneous nodules. Garrod,[30] discussing the relation between erythemas and joint symptoms, remarked that even in rheumatic fever the marginated and papular rashes are more closely associated with articular than with cardiac lesions; whereas chorea and subcutaneous nodules are more likely to be accompanied by endocarditis and pericarditis. However, these observations admit of many exceptions. Thus, although joint symptoms of varying severity were present in 10 of the 15 cases of erythema marginatum recorded in this paper, the eruption antedated or followed articular manifestations at variable intervals; and in at least five instances joint pains were altogether absent, which is not surprising in view of the age incidence (chiefly children). On the other hand, continued observation revealed the practically invariable association of this eruption with evidence of cardiac involvement. Swift noted that the cutaneous lesions occasionally occurred weeks or months before an attack of acute polyarthritis; he also observed instances where the dermatosis appeared months after the arthritis had subsided or had completely disappeared. Barlow saw the dermatosis several times in association with pericarditis, at a time when the joint pains were slight or absent.

In many instances the appearance of cutaneous lesions presaged rise in temperature, but this was variable. In case 8 several crops of erythema marginatum occurred, without appreciable change in the temperature curve. The presence of this eruption seems to indicate rheumatic activity, an observation substantiating the opinion of Swift who believes that the dermatosis represents an important sign of progressive infection, though the process may be only mildly active at the time.

There have been reported a few cases[31, 32] in which erythema marginatum rheumaticum was seen to follow, after variable intervals, a clinical picture interpreted as scarlatina. It would lead too far afield to discuss the alleged relationship between the rheumatic affection and scarlet fever, regarding which opinions differ; the data bearing on this subject have been summarized in another publication.[37] Here it suffices to state that the occurrence of erythema marginatum in such instances, especially where antiscarlatinal serum has not been used, appears to indicate evidence of rheumatic disease; the clinical course of such cases is often an exact replica of ordinary rheumatic fever.

A constant relation between the occurrence of erythema marginatum and severity of course has not been observed by me. It seems that the eruption is found chiefly in classical examples of rheumatic fever revealing undoubted evidence of heart disease. It is the variety most likely to be accompanied by subcutaneous nodules and other frank rheumatic signs. As in the other varieties of eruptions seen in this disease, the prognosis depends for the

most part on the degree and extent of cardiac involvement, and although general rules may be framed, exceptions will undoubtedly be found. However, it would appear that when the dermatosis is disseminated to the extent that unusual sites are affected, for example, the face and dorsa of the hands (Mackenzie,[28] case 5), the outlook seems grave, for in these cases the more widespread distribution of the cutaneous lesions is regarded as evidence of a more serious infection. There may be exceptions to this rule,[77] though the evidence on this point seems suggestive.

Altogether there were three deaths recorded in this group of 15 examples of erythema marginatum rheumaticum. Two of these (cases 5 and 6) are reported at the end of the article. The third concerned a boy, aged 11, in whom the eruption appeared about three weeks before death, which was caused by myocardial failure. Although I have no postmortem data to prove the point, it is probable that the occurrence of the dermatosis indicated rheumatic activity and that necropsy study would have revealed fresh rheumatic changes in the heart as the basis for cardiac insufficiency and death. Bass[38] was probably the first observer to record an instance of erythema marginatum where postmortem examination showed the presence of "myocardial" Aschoff bodies. Several additional examples are recorded in the appended case protocols.

The Dermatological Status of Erythema Marginatum

The question will naturally arise: is this eruption pathognomonic of rheumatic fever? At the present time it seems wise not to be dogmatic. It appears, however, that in childhood the occurrence of cutaneous lesions showing the attributes described may be regarded practically as an evidence of rheumatic fever. For example, Hohlfeld's case,[33] recorded as an instance of "erythema multiforme exsudativum" associated with heart lesions, was in all probability an example of rheumatic fever accompanied by erythema marginatum rheumaticum and subcutaneous nodules; this opinion is based on the clinical description of the cutaneous lesions and the postmortem findings. In young adults, also, this type of eruption seems to be commonly of rheumatic nature. For example, Landouzy and Laederich[34] described, under the title of subacute typhobacillosis, a probable instance of erythema marginatum rheumaticum, characteristic subcutaneous nodules, typical clinical course of rheumatic fever, and equally typical pathologic changes at necropsy.[35] In the succeeding paragraphs the differential diagnosis will be considered at length in an effort to discover how far we may regard the eruption as diagnostic, if not pathognomonic, of rheumatic fever.

(*a*) *Drug Rash:* Salicylate compounds seem not to give rise to lesions of the marginated type, an opinion substantiated by the observations of many writers. Likewise, there is little resemblance between erythema marginatum rheumaticum and the "fixed" eruptions caused by phenolphthalein and other drugs. There seems to be a tendency to overestimate the im-

portance of medication as the origin of rashes seen in rheumatic fever. This may be attributed to (1) the indefinite classification of erythema marginatum rheumaticum, notably in dermatologic nomenclature; (2) reliance on partially performed therapeutic tests which in this case have doubtful significance, as rheumatic erythemas are characterized by rapid involution and subject to numerous recurrences.

(*b*) *"Toxic Ringed Eruptions":* During the course of this study, there came under my observation a few examples of ringed dermatoses of obscure nature, but apparently unrelated to rheumatic fever. These cases revealed lesions disseminated at random over the trunk and limbs. There were numerous irregular rings and gyrate figures showing healthy centers, with circumscribed bright red raised borders. Many such configurations were probably caused by the accidental meeting of curved lines, rather than a result of centrifugal spread from a central point. In some instances fever was present. The clinical course lasted several days in all, with complete recovery. There was no evidence of rheumatic fever. In their morphologic attributes the lesions bore but slight resemblance to erythema marginatum rheumaticum, the latter differing in its predilection for the torso, dull red borders, coppery colored centers, tendency to rapid changes in appearance, recurrences in repeated and numerous crops, and concurrent evidence of rheumatic heart disease.

(*c*) *Serum Exanthems:* In the older literature there are found sporadic reports on so-called *erythème marginé aberrant,* appearing in children following the use of diphtheria antitoxin.[36] These eruptions were described as composed of lesions of variable size, ranging from that of a pinhead to that of a five-franc piece. The centers were flat, unchanged in color, and circumscribed by red raised borders. The lesions spread peripherally and, by coalescence of contiguous patches, arabesque figures were produced. The dermatosis was considered as allied to ordinary urticaria, occasionally succeeding or replacing the latter. Pruritus was pronounced, though less intense and more variable in its occurrence than in true urticaria. In many instances the lesions appeared at the site of injection or at some distance removed from it. More often, there was definite predilection for the limbs, but the eruption gradually spread to the trunk and face. The duration varied from 24 hours to five days. Sequelae were not encountered. Recurrences or repeated crops were uncommon. As in other forms of serum exanthems, the cutaneous manifestations appeared usually within from several days to a fortnight after the initial administration of diphtheria antitoxin, and were generally accompanied by evidence of serum sickness (fever, joint pains, myalgias, lymphadenopathy, gastrointestinal complaints, and occasionally transient albuminuria). From the account furnished by Galitsis, it would appear that these lesions may be differentiated from erythema marginatum rheumaticum by (1) the presence of healthy centers in nearly all instances; (2) lack of recurrent crops; (3) greater tendency to

affect the face; (4) more pronounced itching; (5) tendency to appear at sites of injection; (6) frequently associated cutaneous lesions of polymorphous appearance; (7) concomitant evidence of serum sickness.

The more recent literature contains but few additional reports on this subject.[39, 40] Of 583 eruptions encountered in patients with serum sickness, Goodall[41] found 56.6 per cent true urticaria, 29.8 per cent morbilliform rashes, 12.3 per cent erythema marginatum (circinatum), and the remainder, nondescript erythemas, etc. An interesting point disclosed by Goodall's observations was that, unlike the urticarial and morbilliform varieties, the marginated type was never seen limited to the site of injection but affected a large part of a limb or spread to the trunk and other areas. The latter eruption appeared as early as the fifth day after the use of serum and as late as the twenty-fourth day, with its highest incidence occurring between the ninth and fifteenth days. Since the refinements made in the preparation of serums, the incidence of dermatoses in general has diminished and in particular the marginated variety. As my own observations on serum rashes are chiefly limited to but a few score of cases where tetanus antitoxin, diphtheria antitoxin, anti-pneumococcal serum, etc., were employed, I have encountered no instance of the marginated type, though there were many examples of the urticarial and morbilliform eruptions. Though the appearance of erythema marginatum of serum sickness resembles closely that of erythema marginatum rheumaticum, as indicated in published photographs of the former dermatosis, it is not yet certain that the two are identical in morphology and course. The fact, however, that the administration of serum may give rise to marginated erythemas should be remembered in evaluating clinical and experimental observations. This point will be referred to in another section.

On the other hand, there are cases in which a history of the previous use of serum may be of some importance as regards differential diagnosis. For example, I have notes on the case of a patient whose condition was diagnosed as rheumatic fever accompanied by "papular erythema"; the diagnosis was based on the presence of clinical signs of angina, joint pains, and a functional cardiac murmur. This initial impression was later revised to serum sickness when it was ascertained that diphtheria antitoxin had been injected as a precautionary measure against a streptococcal sore throat. It is therefore possible to err if all the pertinent facts are not assembled.

Transfusion reactions may also be rarely accompanied by cutaneous lesions showing similar attributes, though I have not met with them. This point requires clinical confirmation.

(*d*) *Marginated Type of Erythema Multiforme Exsudativum (Hebra):* Originally segregated by Hebra as a benign cutaneous disease, the systemic nature of erythema multiforme exsudativum was later recognized by Kaposi and others, while Quinquaud added an admirable account of the oral mucous membrane lesions. This condition has been regarded by some as of "rheu-

matic" origin, principally because of the occurrence of joint pains, fever, and cardiac murmurs of probable functional nature, encountered in cases exhibiting systemic features. A more complete exposition of this subject will be found in other publications.[42, 10] Here it suffices to illustrate some of the principles used in evaluating the relation of this dermatosis to the rheumatic affection.

The joint pains encountered in erythema multiforme exsudativum are usually of the nature of arthralgias, designated more properly as "rheumatoid" or "pseudo-rheumatic" for the purpose of differentiating them from true rheumatic articular disease. I have not observed any instances where one could truly speak of fugitive, migrating polyarthritis, though the vast majority of the patients were in the third and fourth decades of life. More important, however, is the cardiac status of these cases. Murmurs are sometimes heard at the apex or base of the heart, but in no instance under my observation did valvular defects result therefrom. The older statistics (Lewin) on the incidence of endocarditis in this condition were compiled at a time when little attempt was made to differentiate the host of conditions included under the generic term erythema multiforme. Moreover, the diagnosis of organic valvular disease was based principally on the presence of a murmur at the apex or base of the heart, in many instances probably of accidental or functional origin. The essential point was recognized by Teissier and Schaeffer [43] who concluded that in many cases of "erythème polymorphe" heart murmurs were "extra-cardiac" in origin; that the incidence of endo-pericarditis was very small; and that, contrary to the opinions expressed by Garrod and Lewin, genuine valvular defects belonged to the rarities. It is likely that the discordance in views may be attributed to the different types of dermatoses studied, for Teissier and Schaeffer were probably concerned with erythema multiforme exsudativum, Garrod, in the main, with rheumatic erythemas, and Lewin, with a heterogeneous group of conditions. No instance of erythema multiforme has come under observation, thus far, where electrocardiographic studies revealed significant alterations, this being equally true of the cases recorded by Meyer as examples of "erythema pustulosum" of rheumatic origin, but which were probable instances of erythema multiforme exsudativum.

The cutaneous lesions of erythema multiforme exsudativum are classified conveniently in two categories, with numerous transitions: (1) erythematopapular type; (2) vesiculo-pustular type. The latter need not be further considered as vesicular or bullous eruptions are but rarely, if ever, seen in rheumatic fever. On the other hand, one of the variants belonging to the first group is the marginated form of erythema multiforme exsudativum which shows resemblances to erythema marginatum rheumaticum; the latter is differentiated, however, by its rapid onset; striking predilection for the trunk; remarkable changes in configuration within short intervals of time, generally measured in hours or days; occurrence in many successive

crops over days, weeks, or even longer; appearance chiefly in children; and in the association with rheumatic stigmas, such as heart disease, subcutaneous nodules, and chorea.

(*e*) *Subacute Bacterial Endocarditis:* A case of "annular edema" was recorded by Lewis and Zotterman [44] in a patient afflicted with subacute bacterial endocarditis. A few cutaneous lesions were observed on the lower limbs and the eruption apparently resembled the urticarial form of erythema marginatum rheumaticum in appearance and course. The interesting experimental observations made in regard to the pathogenesis of the dermatosis will be referred to again. Although the gross postmortem criteria for the recognition of subacute bacterial endocarditis appeared to be fulfilled, a more detailed report of the microscopic findings would have been welcomed, if only to be certain that there was no evidence of concurrent active rheumatic disease. In any event, "annular edema" seems to be a rarity in subacute bacterial endocarditis, for, so far as I could ascertain, it has not been described in this condition by other observers.[45, 46, 47] Neither from personal observation nor from a perusal of about 150 records of cases of subacute bacterial endocarditis can I add another example of a similar eruption. It would seem, then, that only under rare circumstances would this type of cutaneous lesion lead to difficulties in the differential diagnosis between rheumatic fever and subacute bacterial endocarditis, and the possibility that both conditions had appeared concurrently would still remain.[48]

(*f*) *Trypanosomiasis:* It is curious that this disease should give rise to eruptions resembling the rheumatic erythemas very closely. This recalls to mind the old theory, recently resurrected,[49, 50] that the rheumatic affection may be caused by a protozoal agent. Though no conclusions can be drawn merely from the close similarities of the cutaneous lesions, the point seems interesting.

A summary of the essential features of the dermatoses encountered in "sleeping sickness" will be given, the description being based principally on Darré's account [51] and Géry's illustrations.[52] It appears that the several varieties recorded (érythème en placards, érythème circiné) correspond in many particulars to erythema marginatum rheumaticum. Thus, the eruptions are practically restricted to the trunk, only occasionally spreading to the extremities and but rarely affecting the face. The primary element is an urticarial erythematous papule, arranged in discrete lesions, in plaques, or in circinate configurations. The last-named is the most common type, but combinations are often seen. There are no subjective symptoms referable to the lesions. Their duration is variable; sometimes lesions are transient and recurrent, fading in a few days, only to reappear; at other times the erythemas are more persistent, though they vary in intensity from day to day. This eruption was regarded as of diagnostic importance, for Darré observed it in 12 out of 20 cases of trypanosomiasis. It may appear in any phase of the disease, though it usually characterizes the early stages.

The circular lesions may remain unaltered or may coalesce to form polycyclic figures. Serpiginous forms are also encountered. The circular lesions are described as enclosing unaffected skin, but this point was probably a difficult one to determine with precision in persons with swarthy complexions. Examination of the illustrations published by Géry discloses the striking similarities in appearance to that seen in rheumatic erythemas, notably in the serpiginous and polycyclic forms. However, there appears to be at least one fundamental difference, namely, the comparative ease and frequency with which the protozoal parasite can be demonstrated in the cutaneous lesions of trypanosomiasis.

(*g*) *Erythema Perstans Gyratum:* This rare condition which probably includes a number of heterogeneous eruptions, may at times closely resemble erythema marginatum rheumaticum. However, the individual lesions, as denoted by the title, tend to persist, though there appear to be exceptions to this rule. The nature of this group of cases is obscure and there is need for further clinical investigation. The few cases under my observation showed no evidence of rheumatic fever.

(*h*) *Other Marginated Erythemas in Adults:* The subject of marginated erythemas in adults is obscure and complicated. Occasionally true erythema marginatum rheumaticum may be encountered in older persons, as in several examples under my observation. It is more usual to find curious ringed eruptions of unknown etiology (erythema annulare centrifugum, erythema chronica perstans, etc.); these dermatoses are probably unrelated to the rheumatic affection. In some cases, however, the morphologic attributes may closely simulate those of erythema marginatum rheumaticum, though the dynamic characteristics of the latter eruption are usually lacking in the former. In addition, I have encountered two adults who exhibited cutaneous lesions that might have been termed erythema marginatum; these patients were probably not suffering from rheumatic fever. In one, the patches approximated the size of a silver dollar and were symmetrically disposed on the superior and external aspects of the thighs. In the other, the marginated erythema spread over the major portion of the chest in the form of a single large patch, several inches in diameter, with several outlying satellite faint erythematopapular lesions. The course of these eruptions was, perhaps, not as rapidly evanescent as in the case of ordinary erythema marginatum rheumaticum in childhood; yet, there seemed to be definite similarities in appearance and manner of involution. These patients suffered from a febrile joint condition, classified as "acute infectious arthritis"; both recovered completely from the attack, without the production of articular deformities or of organic heart disease. Knowledge of the further course of such cases would be of great interest.

It will be seen, then, that erythema marginatum rheumaticum enjoys its highest degree of clinical specificity in children and young adults. In older persons other varieties of ringed eruption become more common, rendering differential diagnosis difficult.

3. *Flat Erythema Annulare Rheumaticum (Lehndorff and Leiner):* In 1831 and again in 1839 Bright recorded several examples of chorea, accompanied by an eruption which he descriptively termed "roseola annulata." Concerning the rheumatic nature of this rash, little was known, as the conception of rheumatic fever was in a state of flux, the views of Wells, Bouillaud, and others still awaiting general recognition.[8] Almost 100 years elapsed before Lehndorff and Leiner [53] (1922) reported the occurrence of a peculiar dermatosis observed in a small group of children, designating the rash as erythema annulare. They recognized its practically invariable association with endocarditis, the rheumatic etiology of which was not definitely stated until Lehndorff's publication [54] appeared some eight years later. They attempted to differentiate these lesions from "erythema multiforme exsudativum of rheumatic fever." It is evident, however, that the latter was identical with the condition described by Hebra as erythema multiforme exsudativum (preference for limbs, intense bluish-red color, herpes iris, etc.), an affection which is probably unrelated to rheumatic fever, though often confounded with it. In Lehndorff's latest account [55] this interesting error has been rectified.

My study of 24 examples of erythema annulare rheumaticum seems to show that there are transitions to the other varieties of rheumatic erythemas. If the original description given by Lehndorff and Leiner had been strictly adhered to, the number of cases included in this category would have been reduced, for instances intermediary between the flat annular type and the raised marginated variety were grouped together conveniently. When the borders of lesions of the marginated type flatten in the process of involution, the appearance created just before final disappearance cannot be differentiated from the macular variant. As a rule, the former differs from the latter in the greater tendency to "exudative" phenomena (edema and inflammatory cells) in the peripheral portions of the lesions. In addition to morphological transitions, these dermatoses are similar in course, duration, location, and in diagnostic significance. Indeed, Lehndorff and Leiner stated that they had occasionally observed instances of erythema annulare originating from reddish, sharply circumscribed, soft, maculopapular lesions that subsequently flattened into the characteristic ringed erythema as the borders extended centrifugally. It is also evident from Leichtentritt's account that the various ringed forms were included in one category. Although the flat annular and the marginated types are closely allied and in some cases indistinguishable, the merit of having described the variety that is macular at inception belongs to Lehndorff and Leiner. In addition, other interesting features shown by this dermatosis render this differentiation advisable.

The primary element is a flat circular or partially circular lesion several millimeters in diameter. Its color varies from a subdued red to a delicate livid hue. The barely discernible rings are more clearly visible if the patient

remains uncovered a while. The site of predilection is the trunk (chest, abdomen, sides of thorax, and back). Less often, the extremities are involved; no particular favor is shown, however, for the extensor aspects, the flexor surfaces being commonly affected. It appears that the hands, feet, face, and mucous membranes are spared. Within a few hours to days, more usually the former, the circles increase in size and, by coalescence of contiguous lesions, form polycyclic, festooned, and other curiously shaped patterns. The central portions of the rings are colored yellow brown, like chamois skin, whereas the rims contrast by their dull red or violaceous red color.

The extent of the eruption varies from a few discrete efflorescences to almost universal involvement of the trunk, and the distribution is variable with each fresh crop. I have observed instances where isolated patches were localized to the forearms, legs, and buttocks (case 12); it is, however, possible that lesions originally present on the trunk may have been overlooked owing to their transiency.

The course is distinctive. The lesions have a striking tendency to recur in successive outbreaks, each crop having a short duration. The eruption as a whole may be visible several days, but it is more usual to observe complete or incomplete involution in a few hours. As in the case of the other rheumatic erythemas, there are rapid alterations in configuration and development of lesions, these changes occurring from hour to hour or day to day. If one wishes to photograph these dermatoses, it is well not to delay, for the eruption may fade in the interval. In many cases the former sites of lesions are marked by temporary brownish discoloration of skin, which may resemble tinea versicolor, and I have notes on one case where this confusion actually arose. As a rule scaling is absent. According to Lehndorff, hemorrhage with its resultant pigmentation is never seen. However, in rare instances of what appear to be congeners of the localized form of erythema annulare, superficial extravasations of blood may occur, complete involution of the lesions now requiring from 7 to 10 days or longer, as in several cases under my observation.

Lehndorff and Leiner encountered the eruption only in children up to the age of 14 years. Of the 24 cases here reported, the vast majority was seen in patients whose ages ranged from between 3 and 15 years, with occasional instances in young adults up to the age of 21 years. The dermatosis has not been reported in infants, the likely reason being that rheumatic fever is a rarity during this period, but it is probable that such lesions will be found, though uncommonly, in patients below the age of three. Decastello [56] is quoted as having seen the rash in adults with rheumatic fever, but no details were furnished. Recently, I had the opportunity of observing a classical instance in a man, 27 years of age, presumably in his first attack of rheumatic fever. The eruption, of which the patient was unaware, was composed of large circles, up to an inch in diameter, with serpiginous figures

resulting from the meeting of adjacent lesions. The dermatosis was confined to the superior portion of the chest, areas about the axillae, and upper aspects of the abdomen. The clinical picture was featured by the occurrence of fever, articular symptoms, undoubted signs of mitral and aortic valvular disease, electrocardiographic evidence of myocardial damage (prolonged P–R complex, etc.), and the transient eruption. The interesting feature of the rash was the subsequent formation of large circular lesions that were barely discernible to the naked eye, owing to the delicate bluish-pink color of the borders and the faint brownish discoloration of the enclosed areas. In occasional patches, however, the skin seemed to be of normal color. In its appearance and course, the eruption was the counterpart of the type seen in children, except that the diameters of the rings were larger than is commonly observed in erythema annulare rheumaticum.

Despite the paucity of reports on this dermatosis, it appears not to be rare. It is easily overlooked because it is often inconspicuous, discrete, ephemeral, and asymptomatic.

Relation to Active Rheumatic Disease

Lehndorff regarded this eruption as pathognomonic of rheumatic heart disease. Although this opinion is shared by other observers, certain reservations must be made. These reservations do not concern the incidence of heart disease so much as they apply to the actual diagnostic value of the rash. This point will be amplified in the discussion on the differential diagnosis.

According to Lehndorff and Leiner, the dermatosis almost never occurs at the inception of an attack of rheumatic fever, at a time when the temperature and joint pains are most pronounced. As the opportunities to examine patients early in the course are but few, it seems difficult to evaluate the clinical significance of their observation. Moreover, since articular symptoms are generally less intense in children who as a class are more likely to show this eruption, it is not surprising, therefore, that the appearance of these lesions cannot be correlated with severity of articular manifestations. In general, however, the eruption first becomes manifest when the acuteness of the rheumatic process has subsided, but there are exceptions. In some of the cases in the group here reported, there was a short antecedent history of joint pains, and occasionally the cutaneous lesions appeared coincident with relatively acute articular symptoms.

Chorea [54] and subcutaneous nodules [54, 6] have been recorded in association with erythema annulare. I have also encountered several such combinations; thus, in four cases chorea was simultaneously present and in two, subcutaneous nodules. It may be stressed that the occurrence of this eruption in association with chorea is just as valuable as joint pains in seeking substantiating evidence of the rheumatic etiology of "primary" chorea. I have notes on several cases where, had the clinical significance of

this point been known, the diagnosis of encephalitis would have been changed to chorea minor. Lehndorff reported an instance in which erythema annulare was apparently the initial manifestation, the rheumatic nature of the condition being corroborated subsequently by the occurrence of sore throat and endo-pericarditis. In still another example recorded by this observer, the eruption was the earliest sign of a vague febrile illness, which was succeeded by endo-pericarditis and finally terminated in death.

Although erythema annulare usually occurs during a frank recrudescence of rheumatic fever, it is not infrequently seen during intervening afebrile periods. I have encountered two additional instances, not included in the statistics, where the appearance of these lesions pointed to rheumatic disease, substantiated by past history and subsequent clinical signs. In both cases there was no fever at the time of observation, nor were there other obvious symptoms indicating rheumatic activity. One of the patients was brought to me for an obscure eruption and the changes in configuration which were observed with each visit were remarkable. The mother stated that the rash had been present the past few months and that it had been confined to the trunk, the lesions coming and going irregularly. The appearance of the dermatosis with but few evident signs of activity supports the view that in many cases rheumatic fever represents a low-grade process, punctuated by acute exacerbations. The sedimentation time has been observed to be within the range of normal in a few cases; the importance of this phenomenon remains to be evaluated.

Of the three types of rheumatic erythemas, the flat annular form is the one most likely to be found in examples of rheumatic fever featured by indefinite cardiac signs; it is probable, however, that heart involvement in one form or another is present in these cases, but of such nature and extent as to fail to produce typical auscultatory signs. These cases, when followed sufficiently, often develop clinical evidence of mitral stenosis and even aortic insufficiency (case 13). In most instances, however, the cardiac signs are already typical of heart disease by the time the eruption has appeared (cases 14, 15, 16). Occasionally, as in the two examples cited above, it appears that the cutaneous lesions are associated with the more chronic forms of rheumatic disease; in that respect, perhaps, the eruption augurs a favorable prognosis, but at any moment a fresh recrudescence may occur, resulting in death. When the rash appears in a patient showing evidence of congestive failure, its occurrence may be regarded as evidence of activity in the rheumatic process leading to cardiac insufficiency (case 17).

Opinions regarding prognosis in these cases reflect wide differences in fundamental conception. Lehndorff [55] stated that the occurrence of erythema annulare "signifies heart disease"; he observed one fatal case of this sort. On the basis of a study of six patients exhibiting this rash, Abt [1] substantiated this general view; he also encountered one death which supervened some five years after the onset of obvious disease and about one year

after erythema annulare appeared. Perry [6] concluded that the eruption was a good prognostic sign, for in four of the 13 cases of this type recorded by him, all abnormal cardiac physical signs disappeared. On the other hand, Debré and his associates [57] stated that these cutaneous lesions were encountered only in severe cases, "complicated" by endocarditis and accompanied by *Streptococcus viridans* bacteremia; these observers implied a closer relation between rheumatic fever and subacute bacterial endocarditis than is universally accepted. More significant, however, are the statistics furnished by Wallgren [5] who, in a study of 18 examples of erythema annulare in children, found that after a period of observation of several years, five had died at the time of writing and three more showed a heart condition of such nature that "there is hardly any doubt of a fatal ending." Despite these figures, Wallgren noted that the course was unfavorable in all instances and was unwilling, moreover, to regard the eruption as pathognomonic of endocarditis.

Discounting the element of chance which may enter in the collection of material and which may influence the final results appreciably, how can these divergent opinions be reconciled? In studying the relatively large group of cases here reported, it became apparent that the clinical course showed many variations. There were mild cases characterized as chronic active rheumatic heart disease; other instances where the physical signs of cardiac involvement were minimal or apparently absent or disappeared under subsequent observation; still other cases where death occurred during the appearance of the rash or in a subsequent recrudescence. Leaving aside, for the moment, the question concerning the pathognomonic character of erythema annulare, study of this eruption and the other rheumatic erythemas appears to lead, almost inexorably, to the conclusion that involvement of the heart "practically always" accompanies these cutaneous manifestations. The difficulty seems to be in discovering evidence of cardiac abnormalities with the present available methods of investigation. However, when one speaks of absence of involvement of the heart, it is essential that a distinction be made between clinical and pathological criteria, for while the former may be temporarily lacking, the latter seems to be a *sine qua non* for diagnosis. This question will receive further consideration in another section of this article.

The Dermatological Status of Erythema Annulare Rheumaticum

The dictum regarding the specificity of erythema annulare has been upheld by a number of observers.[53, 4, 5, 6, 58] For example, Lehndorff stated that he had not encountered the rash in subacute bacterial endocarditis, rheumatoid arthritis, and articular conditions following scarlet fever, gonorrhea, or syphilis. Kleinschmidt [58] differentiated erythema annulare rheumaticum from the erythema multiforme seen by him in Still's disease and expressed the conviction that the former is absolutely pathognomonic of

rheumatic fever. Yet, until further studies substantiate this important point, it seems the better part of valor to be cautious in drawing this broad conclusion. In the succeeding paragraphs an attempt will be made to establish how far the rash may be regarded as diagnostic of rheumatic fever.

Before discussing the clinical aspects, it seems desirable to introduce a dermatologic distinction. It has been pointed out that it is the rule to find discolored central areas in the lesions of erythema annulare. This appears to constitute clinical evidence that the process is one of centrifugal spread from a central point, the border being the site of most recent activity. On the other hand, there are other unrelated annular eruptions in which the centers of lesions show healthy skin and in which the rings seem to be formed from the very beginning or as a result of the fortuitous running together of adjacent borders. Clinical evidence of extension from a central point appears to be lacking in these cases. Although occasional lesions of erythema annulare rheumaticum may contain apparently healthy centers, my observations seem to indicate that in practically all instances the rings are formed in the manner previously described. Though the distinction is sometimes established with difficulty, the dermatologic nomenclature should provide terms to designate this difference in pathogenesis.

(*a*) *Drug Eruptions:* The observations recorded by Lehndorff and Leiner indicate clearly that the flat annular erythema rheumaticum bears no relation to ingested drugs, such as sodium salicylate, quinine compounds, pyramidon, etc. I have notes on one case where eruptions due to nirvanol and to rheumatic fever occurred successively in the same patient, affording the opportunity of comparing them with one another and of noting the essential dissimilarities.

(*b*) *Cutis Marmorata* (*"Marbled Skin"*): Tachau [42] was of the belief that erythema annulare rheumaticum is identical with "marbled skin." Although both conditions are more conspicuous after the skin remains uncovered a while, the former is so distinctive, once seen, as to render differential diagnosis more theoretical than practical. Yet, it seems advisable to suggest caution in diagnosing this eruption following the use of such procedures as hot baths, etc.

(*c*) *Still's Disease:* Erythematous eruptions have been recorded occasionally in Still's disease, regarded by most observers as the juvenile equivalent of rheumatoid arthritis. Bolders [59] described a typical example of the condition, in which an evanescent macular erythematous eruption appeared on the extensor aspects of the limbs; the dermatosis was at first regarded as a drug rash, but the subsequent course spoke clearly against this belief. In discussing Bolder's case, Langmead [60] stated that he had seen similar dermatoses in several examples of this disease, the lesions being papular, dusky red, and exhibiting a tendency to localize about the joints; he cited a typical instance of Still's disease in which cutaneous lesions appeared during many febrile exacerbations occurring over many years. Bailey [61] also re-

corded an instance in which a mild erythema, composed of flat and slightly raised lesions, occurred on the arms each night and generally faded by the following morning; the eruption was diagnosed as erythema multiforme and considered as a manifestation of streptococcal infection. Kleinschmidt [58] mentioned the occurrence of transient erythematous eruptions in Still's disease but he was convinced that these were entirely different from erythema annulare rheumaticum. I have recently observed an apparent exception to this rule in a boy five years of age. His illness, which began nine months before, was regarded at another institution as rheumatic fever; electrocardiograms showed simple, non-paroxysmal tachycardia and acute myocardial damage (?) due to rheumatic heart disease. During the time I observed this case the outstanding features were fever reaching a peak of 105° F., polyarthritis, indefinite cardiac murmurs, and an erythematous rash on the abdomen and back, the lesions appearing with elevations in temperature. A distinct pericardial friction rub was heard at one time. There was generalized lymphadenopathy of moderate grade. The eruption was composed of efflorescences colored a delicate pale pink, with central clear areas that occasionally showed a faint brownish hue. The transiency and appearance of the rash were similar to erythema annulare rheumaticum. During the course the pericardial friction rub disappeared, the fingers became spindle-shaped, the wrists and knees enlarged somewhat, the lymphadenopathy became more pronounced, and the general clinical picture of Still's disease seemed to be produced. However, splenomegaly was not present clinically and on several occasions electrocardiograms revealed abnormalities (inversion of T_2 and T_3, notched QRS complexes). Although it seemed reasonable to classify this case as one of Still's disease, further observation is essential owing to the fact that many features appeared to point to rheumatic fever. Complicating the problem is the belief of several observers, notably of the French school, that there exists an endocarditic form of Still's disease; the evidence on this point, however, seems tenuous at present. Should further observation fail to reveal essential differences in the appearance and evolution of the rash seen in this condition, the clinical specificity of erythema annulare rheumaticum would depreciate. In any event, the resemblances in cutaneous lesions cannot be used at present to corroborate the hypothesis that Still's disease and rheumatic fever are caused by the same agent, for the weight of clinical and pathologic evidence seems to militate against this view. It is, however, important to note the great clinical difficulties encountered in differentiating these conditions from one another, especially in the early stages, and the case just cited must be evaluated in that light.

(*d*) *Erythème Marginé Aberrant of Grippe:* Various types of ephemeral erythemas have been encountered in epidemics of grippe.[62] In general, most of the reports concerned with this subject have been of an eclectic nature. Among the eruptions described only that reported by Jacquet [63]

stands out as likely to be confounded with the rheumatic type. Jacquet observed 10 cases of grippe exhibiting a dermatosis characterized by rose-colored macular lesions of circular configuration. The rings spread peripherally, forming large central zones of livid tint, up to a five franc piece in size, and circumscribed by flat borders. The eruption usually appeared on the second day of illness, developed rapidly, and persisted throughout the febrile period. The distribution of the dermatosis varied, lesions having been observed on the limbs (feet, hands, palms), especially on the extensor aspects, and also on the trunk. On the latter part of the body large arabesques were formed from coalescence of patches. Jacquet pointed out the similarities between this eruption and that seen following the use of diphtheria antitoxin,[36] the only striking difference being that the former showed lividity of the central areas of lesions. From the descriptions at hand, there appear to be close similarities to the flat annular erythema of rheumatic fever, though the latter displays greater tendencies to repeated crops and special favor for the trunk. If it should be demonstrated that Jacquet's dermatosis is indeed the clinical counterpart of the rheumatic type and that it occurs with some frequency in epidemic and endemic grippe, the specificity of the latter eruption will again be depreciated. It is, however, important to note the following points: (1) there is a tendency to group many conditions under the generic category of "grippe," a diagnosis often arrived at on the basis of exclusion; (2) I have observed instances of rheumatic fever with transient erythemas of the types already described, the clinical course having been ushered in by a series of upper respiratory symptoms commonly called "grippal." It seems, then, that considerable caution should be exercised in designating an eruption as a grippe exanthem, unless the patient has been followed sufficiently to exclude, with reasonable certainty, the diagnosis of rheumatic fever.

General Features: Clinical and Experimental Applications

An attempt has been made to segregate what may be termed the genuine rheumatic erythemas. To this end strict criteria have been invoked for the diagnosis of rheumatic fever and of rheumatic dermatoses. Besides the diseases mentioned in the opening paragraph, the following erythematous eruptions have been excluded: erythema nodosum, Osler node, psoriasis, scleroderma, dermatomyositis, systemic lupus erythematosus,[2] and erythema elevatum diutinum. It is my belief that the rheumatic nature of these conditions has been advocated on the basis of doubtful criteria, insufficient data, incomplete observation, disputed conceptions, or coincidence of conditions.

Analysis of the rheumatic rashes discloses many points of general interest. As in the case of the other manifestations of this disease, they share similar ephemeral qualities, the lesions coming and going irregularly, with wide fluctuations in intensity. In comparing reports issued from many countries, it seems noteworthy that the clinical features of rheumatic fever

were, with but rare exceptions, very much alike; the differences appeared to be related more to minor variations in clinical course and to individual interpretations. This was found to be true, also, in the case of the erythemas and the subcutaneous nodules. It seems, then, that there is no reason to believe the disease differs fundamentally when seen, for example, in New York City, England, or in France. One of the most disputed points is that concerned with the incidence of cardiac disease in rheumatic fever, a consideration of which is pertinent to the evaluation of the cutaneous lesions observed in this condition.

It has been said that the heart is more likely to be involved in children, whereas articular manifestations are apt to be more pronounced in adults. These general rules admit of many exceptions. MacCallum [64] found that the cardiac derangements were identical in all age groups. It is probable that involvement of the heart in one form or another is a constant feature of the condition in both children and adults,[16] a fundamental view that appears to be gaining ground. Thus, Bezançon and Weil, utilizing several methods of approach to the problem, concluded that "The cardiopathy is the outstanding manifestation of rheumatic disease. *It is constant.* It is to this feature that the affection owes its special character." Still more recently, Bezançon stated: "Observers can no longer consider it (cardiac involvement) as a complication; *it is the disease itself.* . . ." Considering the present, more refined methods of discovering abnormalities of the heart, the exceptions to the statement formulated by Bezançon will probably become less common. If this is true, the views of Bouillaud, framed on insufficient and partially erroneous grounds, will be resurrected. Occasionally the valves of the heart may be so slightly damaged that fairly complete healing takes place, without the detection of murmurs during life.[67] Rarely, gross examination of the endocardium reveals that it is spared, yet microscopic study discloses marked interstitial valvulitis.[68, 69] At times the only evidence of rheumatic disease may be the "myocardial" Aschoff body.[70]

Microscopic studies appear to indicate that rheumatic fever has a marked aptitude for damaging collagenous tissue throughout the body (fibrinoid swelling of Klinge,[71] Aschoff body, fibrinoid degeneration of vessel walls etc.). Of the changes mentioned, only the "myocardial" Aschoff body is regarded in many quarters as pathognomonic of the condition.[16, 48, 72, 73] This view has gained wide acceptance, notwithstanding Klinge's observation that the well-constituted Aschoff body represents the changes of an advanced pathological process, rather than the earliest morphologic expression of the disease. This characteristic structure, the specificity of which seems, thus far, to have been demonstrated principally for the heart, is found in over 90 per cent of the acute cases (usually acute exacerbation), but in only 15 per cent of instances showing chronic rheumatic cardio-valvular disease.[74] Fahr [58] claims its constant occurrence in children, using this as an important differential point. If, after prolonged search, no evidence of the Aschoff

body is forthcoming, it becomes essential to invoke other morphological criteria, consideration of which would be beyond the scope of this article. With the possible exception of the subcutaneous nodules found in the *galea aponeurotica*,[75, 76] there is at present no unanimity of opinion regarding the significance of the structural changes found in these lesions; for example, Saphir and Wile [48] regarded these microscopic alterations as non-specific.[37] So far as the true cutaneous lesions are concerned, no one seems to have demonstrated the occurrence of genuine Aschoff bodies in the skin, so that the absence of these structures in this type of material does not militate against a possible rheumatic origin. On this point, however, observations have been scant.

It has not been shown conclusively that the "fibrinoid" degeneration or swelling described by Klinge as the "primary infect" is peculiar to rheumatic fever alone, especially when found in organs other than the heart. Both Aschoff [78] and Fahr [79] and, more recently, Saphir and Wile pointed out that the structures depicted by Klinge are of themselves inconclusive for the diagnosis of rheumatic fever *sensu stricto*. It appears that a similar view may be held to apply to the numerous types of vascular alterations recorded thus far.[80] These controversial points are mentioned, as such evidence is often presented in connection with cutaneous lesions regarded as of "rheumatic" nature; if, however, such observations are scrutinized closely, it is found that the term "rheumatic" has been broadly interpreted.

The establishment of postulates for the recognition of this disease in the manner prescribed by the New York Tuberculosis and Health Association [15] represents a step forward in the critical evaluation of cutaneous manifestations formerly classified in the rheumatic category. When it is stated, for example, that an eruption appeared in the absence of clinical evidence of heart disease and that several months later, undoubted physical signs of a "sclerosing" type of mitral stenosis became manifest, it seems likely that the valve in question had been damaged previously, without having given rise to typical murmurs. When, on the other hand, a patient suffers from six attacks of "rheumatism," of which four are accompanied by an eruption, and at postmortem examination no evidence of cardiac abnormalities are discovered, it seems unlikely that the condition was really rheumatic fever in its strict sense.

Although it appears that evidence is accumulating with respect to the "practically" invariable occurrence of cardiac involvement in one form or another, there are instances where the clinical and laboratory aids to diagnosis are not sufficiently delicate to detect changes of a minor grade. It is on this basis, principally, that the view has arisen relative to the facultative occurrence of heart disease in rheumatic fever, notably in the case of adults. Many authorities have demonstrated the occasional discrepancies between clinical diagnosis and postmortem findings.[81, 82, 83] Two interesting examples bearing directly on the problems with which this paper is concerned

were recorded by Weber [85] and Wyckoff and Bunim [86]; these cases illustrate the necessity of using additional methods in order to arrive at reliable conclusions, though the latter procedures also have their limitations. Electrocardiographic and fluoroscopic changes may be absent in the early stages of rheumatic fever or in mild cases of the condition; concerning these and other methods of investigation, their precise value in the diagnosis of incipient rheumatic disease remains to be determined. The most decisive evidence of the rheumatic nature of any particular case will be found post mortem in detailed studies of the heart.

On the other hand, those who would eliminate the possibility of rheumatic fever because the heart is apparently not involved, must carefully distinguish between clinical and pathological findings. The critical evaluation of functional murmurs is only mentioned in passing, but this has been one of the chief sources of error in considering the etiology of cutaneous lesions.[87] As far back as the middle of the nineteenth century there were observers who recognized that absence of clinical evidence of heart disease "is no proof that there is no valvular involvement." (Oxley,[65] Hillier.[66]) Osler averred that during an attack of endocarditis there may be no audible cardiac murmurs, yet the foundation for future trouble is established at that time; this belief was based on postmortem examinations, as previously cited. On the other hand, several investigators (Wollenberg,[84] Castren [90]) have noted the delicate structure and localized distribution of the valvular vegetations encountered at necropsy in cases of fatal chorea, where death was not caused by cardiac failure. On the basis of analogy the view has been advanced that the verrucae may heal completely in mild instances of rheumatic fever, without at any time giving rise to embarrassment to the pulmonary circulation; postmortem examinations would appear to support belief in the existence of this mild type of disease. Knowledge of the rheumatic cutaneous lesions may be of aid in evaluating studies undertaken from this point of view. It is, however, probable that even in the event of "complete healing," examination of the heart post mortem would reveal macroscopic or microscopic changes of antecedent disease, provided the patient had been afflicted with rheumatic fever.

These data appear to explain the variability in the prognosis of rheumatic fever. Though the heart may be involved in all cases, the extent and distribution of the pathological changes determine the outlook, aside from other uncommon factors and complications which may play a part. In nearly all the cases exhibiting rheumatic cutaneous lesions there was already evidence of involvement of the cardiac structures in one form or another; when this evidence was absent, subsequent observation disclosed that the heart had been implicated in the process, with but rare exceptions. Where postmortem examination was performed, the findings of rheumatic heart disease were encountered, though these were variable in severity. Study of the eruptions seemed to furnish some clue regarding the degree of cardiac

involvement, but these rules were not without exceptions. Thus, the simple papular type appeared to be associated with relatively mild cases of rheumatic fever, death being uncommon in the immediate attack, as judged by my observations and those extant in the literature. The marginated type was found in what might be termed the average textbook picture of rheumatic fever, exhibiting undoubted evidence of heart disease, and it was not uncommonly accompanied by the occurrence of subcutaneous nodules; death may occur, particularly when the eruption spreads beyond the ordinary sites of predilection. Any extraordinary distribution is to be regarded apprehensively as an evidence of severe "toxemia." The flat annular type was the variety most likely to be encountered in instances characterized by prolonged course (chronic active rheumatic fever). As there were transitional instances and some exceptions these observations must be taken advisedly until further studies are undertaken.

Analysis of the rheumatic dermatoses revealed evidence substantiating two general beliefs: (1) that rheumatic fever is often a chronic recurrent process, punctuated by acute exacerbations; (2) that cardiac failure in these patients, commonly attributed to mechanical factors, was in most instances actually the result of continued and progressive rheumatic activity. On the other hand, it appeared that these eruptions presented clinical attributes vastly different from those seen in the cutaneous lesions accompanying infections caused by *Streptococcus viridans* (alpha), *Streptococcus hemolyticus* (beta), *Streptococcus anhemolyticus* (gamma), and the enterococcus; that this may be explained on the basis of the variable response termed "allergy" is an hypothesis which, though reasonable, requires substantiation and clarification. The subject of allergy in relation to rheumatic fever and its erythematous rashes will be alluded to briefly in another section of the paper.

Study of the rheumatic eruptions reveals that though the question of nosology is of some importance, there are numerous other problems, concerning which our fund of knowledge is meager. These questions are of interest as they indicate future lines of investigation.

(*a*) *Histopathology:* So far as I could ascertain, there is but one report published concerning the histopathology of the rheumatic erythemas, an example of erythema annulare described by Carol and Krieken.[88] They found that the lesion showed a cellular infiltration, composed mainly of polymorphonuclear leukocytes, distributed chiefly about dilated vessels in the papillary and subpapillary zones. The infiltrate also was dispersed in the adjacent and intervening areas. The elastica and collagen bundles were preserved. No bacteria, including the tubercle bacillus, were found. These observers differentiated this histologic picture from that seen in ordinary annular urticaria and erythema multiforme exsudativum, and their paper represents a laudable attempt to segregate erythema annulare from simulating dermatoses. It is, however, clear that until clinical differentiations of

the vast group called "erythema multiforme" become established, histologic studies will be less valuable unless the condition is as sharply demarcated as in the report by Carol and Krieken. Under the guidance of the late Dr. Louis Gross, I had the opportunity of examining sections of a case of erythema annulare, and, as the biopsy was performed by me, I was able to correlate the clinical with the histologic features. In the main I can confirm the findings recorded by Carol and Krieken, except that there was observed a certain rough attempt at "palisade arrangement" of the cellular infiltration in areas and many of the polymorphonuclear leukocytes appeared to be fragmented. Edema about the vessels, though present, was not striking and there was no obvious evidence of collagenous degeneration. Eosinophiles were not more numerous than normal. As this study was brief and interrupted, I was unable to determine the nature of the central discoloration observed in this lesion (hemosiderin?, melanin?). It is of great interest that the cellular reaction was of an intensity far out of proportion to what one would expect, considering that the lesion intra vitam was flat, with hardly any evidence of marked activity.

The rheumatic nature of the two cases cited was based on clinical grounds. The pathologic changes appeared to show features that do not conform to the Aschoff body as observed in the heart. A similar view is held in regard to the subcutaneous nodule, with the possible exception of those found in the *galea aponeurotica*. The observation that various tissues seem to react differently to the rheumatic "poison" is apparently upheld by these studies, but the question still remains of whether this is due to individual inherent properties in the organ attacked. In any event, further observations may determine whether the pathologic alterations found in the skin of these cases are characteristic or pathognomonic. My belief is that these changes will be regarded as non-specific, but that these features will serve as valuable means of making a diagnosis by exclusion.

Vesicular and bullous lesions are rarely, if ever, encountered in rheumatic fever. The few instances recorded seem not to possess the stamp of authenticity, if analyzed in terms of the criteria set forth in this paper, and their probable classification will be discussed in another publication. Considering the marked degree of "exudation" described above, it seems surprising that vesicles or even bullae are so uncommon. This can be explained on two grounds: (1) the degree of edema is not very intense, and there is a restricted capacity to infiltrate the epidermal layers; (2) more important is the clinical attribute of transiency displayed by these lesions, which indicates that the "poison" reaching the skin is rapidly diffusible and quickly dissipates itself.

(*b*) *Bacteriology:* Reports on the bacteriologic findings in the rheumatic erythemas are scant. There are, however, a few observers [20, 51] who stress the possibility that *Streptococcus viridans* is the etiologic agent in these cases, implying thereby a very close relation between rheumatic fever

and subacute bacterial endocarditis. There are so many discordant views regarding the significance of bacteriologic results obtained from cultures of skin that whatever data are accumulated along these lines should be subjected to extremely rigorous control and evaluation. There seems little likelihood that the common aerobic organisms will be found to be of significance, so far as the rheumatic rashes are concerned, especially if the "allergic" hypothesis is correct. The claims put forward for any of the various streptococci still need substantiation. The resemblance of the rheumatic erythemas to the cutaneous lesions reported in trypanosomiasis is mentioned again for the purpose of calling to the attention of the investigator the possible importance of higher bacteria, in particular protozoal agents.

(*c*) *Epidemiology:* Knowledge of the rheumatic dermatoses should be of value in estimating conclusions drawn from epidemiologic investigations of the type pursued by Paul and Salinger.[89]

(*d*) *Therapy:* If the hypothesis that *Streptococcus hemolyticus* is the cause of rheumatic fever should prove to be correct, the use of sulphanilamide should prove of value in the treatment of rheumatic fever, provided that no complicating factors interfere with its direct action. It will be interesting to observe the effect of this drug on the evolution of the rheumatic eruptions. Preliminary observations by Swift [77] appear to indicate that sulphanilamide is of doubtful value in preventing or aborting the appearance of these dermatoses as well as of the subcutaneous nodules.

(*e*) *Experimental Studies:*

1. *Streptococcal "Nucleoprotein":* Coburn, using streptococcal "nucleoprotein" intracutaneously, was able to reproduce erythema marginatum, the lesions appearing especially about the sites of injection as well as other parts of the body. Although in some of the cases cited by him there were marked similarities in appearance to erythema marginatum rheumaticum, it seems more probable that the dermatosis produced by this means stands in closer relation to the variety found in serum sickness. It is possible that histologic studies may uncover criteria whereby to differentiate these dermatoses from one another.

2. *Histamine Studies:* The experimental work carried out by Lewis and Zotterman [44] on "annular oedema" is of great interest in respect to the problem of pathogenesis. They observed that when the centers of lesions were stroked or injected with adrenalin, there was a normal whealing response; on the other hand, the injection of histamine produced little or no whealing, indicating that the blood vessels in these areas were refractory to that substance. These results conformed with those obtained by Lewis in previous experiments on the phenomenon of wheal formation in damaged skin, the latter showing a peculiar state of refractoriness to the further injection of histamine. This principle has been made the basis for an interesting hypothesis explaining certain configurations assumed by cutaneous lesions. Using similar procedures, Perry [6] was unable to demonstrate a

refractory state to the injection of histamine, but the eruption studied by him was erythema annulare rheumaticum in which, as a rule, whealing does not often occur as compared with erythema marginatum rheumaticum. On clinical grounds, however, there appears to be much evidence that erythema annulare arises from a central point which extends centrifugally in the same manner as that described by Lewis and Zotterman in their case of "annular oedema." This principle concerning the evolution of lesions will be found to be exemplified by many types of dermatoses and it is possible that the underlying basis may be the liberation of histamine or histamine-like substances. While Lewis and Zotterman attached little importance to the naming of the cutaneous lesions described by them on the ground that it "brings us no nearer an end point," it seems doubtful whether real progress will be achieved until the eruptions in question are properly designated, for, although the principle of pathogenesis may be the same or much akin, clinical differentiations will also be important in understanding what is being studied. The golden mean lies between the descriptive phase introduced by Hebra and the modern tendency to discover etiology and pathogenesis, and it seems unlikely that the latter will ever be independent of the former.

3. *Reproduction of the Disease in Experiments on Animals:* If the cutaneous lesions of rheumatic fever contain or are produced by the etiologic agent of the disease, the advantages accruing from the use of such material which can be obtained intra vitam would be manifest in experiments on animals. Unlike the subcutaneous nodule which usually requires a period of time before it becomes visible, the rheumatic eruptions present themselves almost immediately. Despite the present belief of many investigators regarding the "allergic" nature of these dermatoses, studies of this type appear to be worthy of trial.

4. *Skin Tests:* The development of a reliable skin test in rheumatic fever would mark a significant advance in the study of this disease and in the ferreting out of the mild and the very early cases of the condition. Thus far, all efforts to develop such a test on practical lines have proved fruitless, including some experiments carried out by the late Dr. Louis Gross and me, utilizing a number of different extracts of tissues obtained from fatal cases of rheumatic fever. It would be interesting to use extracts of skin taken from sites of rheumatic erythemas; if this is difficult to obtain, blister fluid (cantharides or other irritants) might be employed.

It will be seen, then, that while knowledge has been accumulated on the subject of the rheumatic erythemas, much remains to be done.

Case Reports

Case 1. Child aged 10; chorea; epistaxis; fever; mitral stenosis and insufficiency; pericardial effusion; crops of cutaneous lesions; subsequently, myocardial failure.

P. C., girl aged 10, was first seen July 23, 1930. Three months prior to admission she had an attack of chorea. Three days before hospitalization she complained of fever, epigastric pain, and epistaxis.

On examination physical signs of mitral stenosis, mitral insufficiency, and pericardial effusion (subsequently confirmed by roentgenogram) were noted. An electrocardiogram revealed a P–R complex measuring 0.20 sec. Temperature ranged between 102° F. and 103° F., but gradually assumed a normal level. After an afebrile period of two weeks, the temperature rose to 100.5° F. and an erythematopapular eruption appeared over both elbows, mainly on the extensor aspects. The cutaneous lesions were dull red papules arranged discretely and in patches. In a short time the eruption underwent involution, but several days later a few similar lesions appeared on the buttocks. This crop was also transient. At no time were there subjective symptoms referable to the rash.

She was seen again August 25, 1931, with an unmistakable recrudescence of rheumatic fever. Physical signs of mitral stenosis, mitral insufficiency, and adhesive pericarditis were present. There was evidence of congestive heart failure. An electrocardiogram revealed notched P-waves in all leads. One year later similar physical signs were noted.

Case 2. Previous attack of rheumatic fever; entered with swollen joints, fever, tachycardia, and eruption; mitral stenosis and aortic insufficiency; leukocytosis; electrocardiographic changes; confusion with salicylate eruption; recurrent crops of cutaneous lesions and articular pains.

A. K., boy aged 17, was first seen June 24, 1931. Ten years before admission, he had a febrile illness accompanied by painful swollen joints. Since then he had suffered from dyspnea on exertion, and, on one occasion, from precordial pain. The recent symptoms began two weeks before hospitalization when he noted pains in the knees, later associated with stiffness of these articulations. After a few days the knees, ankles, and toes became swollen.

On examination there was observed an erythemato-urticarial eruption situated over the left lower quadrant of the abdomen. Physical signs of mitral stenosis, mitral insufficiency, and aortic insufficiency were noted. There was moderate leukocytosis (12,800). An electrocardiogram revealed a P–R complex measuring 0.21 sec.

In about two days the cutaneous lesions disappeared, though joint pains were still present. July 31, the eruption reappeared on the abdomen, without being accompanied by rise in temperature; this crop faded within 72 hours. Despite the use of large doses of sodium salicylate, the polyarthralgias persisted. Sedimentation time was 15 minutes (Linzenmaier method). Fluoroscopic examination revealed an enlarged left auricle, pulmonary conus, and left ventricle. August 13, there were mild pains in the knees, elbows, and ankles, without any rise in temperature. Within 24 hours the abdomen, loins, and inguinal regions were sites of isolated and confluent reddish papular lesions. The diagnosis of erythema urticatum due to salicylates was suggested. By the following day the eruption began to fade. The rash was interpreted, however, as of rheumatic nature, for simultaneously fever and tachycardia appeared, accompanied by increased severity of the arthralgias. Several days later there was a recurrence of the rash on the abdomen, again accompanied by fever and tachycardia. On the following day salicylate therapy was stopped. At this time the rash was no longer present.

During the next four days there was a fresh febrile attack associated with generalized articular pains. The metacarpo-phalangeal joints of the second and third fingers of the left hand were swollen and tender. Several days later sodium salicylate was administered in large doses, resulting in diminution in the intensity of the articular pains and lowering of the temperature to normal. September 8, the patient was practically asymptomatic; pulse rate 80 to 90; sedimentation time 50 minutes. There had been no recurrence of the eruption despite the administration of sodium salicylate in large doses.

One year after discharge, the patient was found to be "well compensated." In

the interim he had experienced occasional attacks of palpitation and dyspnea on exertion of a mild type.

Discussion. It is likely that the eruption represented an example of erythema papulatum rheumaticum in which the lesions had been confined to the abdomen and the urticarial component clinically pronounced. In favor of a rheumatic origin were the transiency, occurrence in crops, and association with signs of activity in the rheumatic process on several occasions. While the possibility of salicylate rash was suggested, this could be eliminated since the eruption had been present on admission before any use of the drug, had disappeared and reappeared independently of its administration, and had failed to recur on the last occasion when this medication had been resumed in large doses.

Case 3. Previous vague history of rheumatic fever with recurrent crops of erythema; on admission: fever, joint pains, mitral stenosis, mitral insufficiency; leukocytosis; crops of erythema papulatum and marginatum.

I. G., boy aged 9, was observed July 11, 1934. Two years prior to admission he had vague pains in the arms and legs, accompanied by slight fever. The joints were not swollen. Since then, he had experienced occasional sore throats. One week before hospitalization he complained of pain in the right knee; there was no swelling or redness of the part. An erythematous, non-pruritic eruption appeared on the arms and legs, the lesions disappearing and reappearing several times.

On examination physical signs of mitral stenosis and insufficiency were noted. The tonsils were hypertrophied. On the extensor aspects of the arms and legs and, to a lesser extent, on the flexor surfaces of the arms, there were fading maculopapular erythematous lesions, some discrete, others in confluent patches. Pruritus was absent. There was moderate leukocytosis (16, 600). The temperature was 101° F. On the following day the articular pains disappeared. Two days later a profuse eruption appeared on the buttocks, lower part of the back, and on the upper and lower limbs. This was composed of discrete lesions and confluent patches of erythematous papules and interspersed marginated lesions ranging up to an inch in diameter. The individual efflorescences had a pronounced urticarial component, but itching was not a complaint. Two days later the temperature curve assumed a normal level. The cutaneous manifestations fluctuated in intensity but soon began to undergo involution.

Discussion. Although this was not a full-blown example of rheumatic fever, the presence of cardiac abnormalities, articular pains, fever, leukocytosis, and the type of eruption appeared to favor this diagnosis.

Case 4. Woman of 37; several antecedent attacks of rheumatic fever; roentgenologic changes in small joints of fingers; erythema papulatum; differential diagnosis between rheumatic fever and rheumatoid arthritis; differential diagnosis between rheumatic rash and salicylate eruption; mitral stenosis and insufficiency; electrocardiographic changes.

M. B., woman 37 years of age, was first seen in 1924. At that time she gave the history that, following a miscarriage and curettage in 1920, she developed swollen painful joints accompanied by fever and sweats. Since then, she suffered from dyspnea, palpitations, and fleeting articular pains. Following childbirth in 1924, she had an acute exacerbation of her illness, manifested by pains in the joints, dyspnea, and palpitations. There were physical signs of mitral stenosis. An electro-

cardiogram revealed left axis deviation, with abnormal R–T transitions in the first and third leads. The temperature was subfebrile for three days, then fell to normal for the remainder of the period of observation.

She was seen again February 7, 1930. Five weeks before this, she was exposed to inclement weather, following which she complained of a feeling of chilliness, headache and sore throat. Two days later there was pain in both ears, but the condition subsided spontaneously. This was followed by a chill, the temperature rising to 105° F. The right knee was swollen and painful. In rapid succession the ankles, wrists, and interphalangeal joints were implicated, the process subsiding in one joint and commencing in another, with several recurrences. She complained of pain and stiffness in the neck, associated with profuse perspiration, moderate dyspnea, and palpitations.

On examination physical signs of mitral stenosis and insufficiency were noted. The knees, right wrist, and interphalangeal joints of the left index finger were tender to touch, warm, and painful on movement. There was moderate leukocytosis (13,000). The clinical course was characterized by successive involvement of many joints, each subsiding in a short time, only to be followed by a fresh attack in other articulations. The temperature curve was remittent in type. Salicylate therapy was instituted. Subsequently a localized, dull red, papular eruption appeared on the right buttock and left forearm, the lesions fading in 24 hours. Salicylate therapy was discontinued on the hypothesis that the dermatosis was of drug origin, and the rapid involution of the rash was considered substantiating evidence for this opinion. However, I later ascertained that through an error the administration of the drug had been continued for three days after the initial appearance of the eruption. In other words, the cutaneous lesions disappeared spontaneously despite the continued use of the medication. Two days after the actual discontinuance of the drug, pains in the joints recurred. Because of the painful swollen articulations of the fingers and because a roentgenogram revealed slight hypertrophic changes in most of the small joints of the hand, the opinion was advanced that the case was one of infectious arthritis, non-rheumatic in nature.

Discussion. It is my belief that the characteristics of the eruption favored the diagnosis of rheumatic fever, rather than "infectious (rheumatoid) arthritis." The following additional evidence may be cited. Aside from definite electrocardiographic changes noted during the first period of observation, subsequent studies revealed P–R complexes ranging from between 0.21 sec. and 0.24 sec. on several occasions. The remittent type of fever, leukocytosis, character of the articular manifestations, response to salicylates, and the cardiac abnormalities were consonant with this belief. Implication of small joints is a phenomenon that is not entirely restricted to rheumatoid arthritis; in the latter condition the smaller articulations are usually involved first and in a more symmetrical and permanent manner than occurred in this case. The disappearance of the rash during the accidental continued administration of sodium salicylate is a point definitely militating against the assumption of a drug origin; likewise, the involution of the cutaneous lesions in less than 24 hours, a common occurrence in the case of the rheumatic erythemas, would have been most unusual for a salicylate rash. The localized distribution and transiency of the eruption, comparable to the fleeting symptoms of rheumatic fever, are attributes to be stressed.

Case 5. Boy aged 3; first observation: crops of subcutaneous nodules, fever, mitral stenosis, electrocardiographic changes, erythema circinatum; second observation: crops of erythema marginatum; third observation: fever, joint pains, crops of erythema marginatum, crops of subcutaneous nodules, transformation of peculiar urticarial lesions into erythema marginatum, death; postmortem findings: acute and chronic rheumatic cardio-valvular disease, Aschoff bodies in heart.

C. S., boy aged 3, was first seen March 14, 1930. About six months before this, the child took ill suddenly, complaining of pain in the left leg and sensation of fever. Subcutaneous nodules appeared all over the body, but disappeared within a few days. He was acutely ill for two weeks, when a cardiac murmur was heard for the first time. He became pale and began to lose weight rapidly. One week before hospitalization several crops of nodules appeared in rapid succession on the hands and over other parts of the body.

On examination physical signs of mitral stenosis and insufficiency were noted. There were numerous subcutaneous nodules on the elbows, ankles, vertebral spines, scapulae, metacarpo-phalangeal joints of the right hand, and scalp. There was moderate secondary anemia. An electrocardiogram revealed prominent P- and T-waves and abnormal R–T transitions in the first and third leads, interpreted as indicating myocardial damage. The subsequent course was characterized by the occurrence of numerous crops of subcutaneous nodules, afebrile temperature except for an occasional rise to 101° F., development of left pleural effusion, and the occurrence of a faint brownish red annular erythema located on the lower part of the back and gluteal regions.

The child was seen again some three years later. From time to time a few erythematous blotches would appear on the skin. Shortly before the second observation he had epistaxis, sore throat, fever, and pain in the feet. Dyspnea and orthopnea became prominent symptoms. A generalized erythematous rash appeared on the trunk, the eruption being moderately pruritic and disappearing in a few days. On examination the patient seemed acutely ill. Lips and fingers were cyanosed. Temperature was 103.4° F.; pulse rate 130. The abdomen and chest were sites of a generalized erythematopapular rash composed of marginated lesions, the diameters of which ranged from between 8 and 10 cm. The borders of the lesions were raised and colored pink; the centers had a peculiar yellowish brown hue. There were scattered interspersed discrete erythematous papules. Physical signs of mitral stenosis, mitral insufficiency, and fibrinous pericarditis were noted. The clinical course was stormy and characterized by periods of high fever, development of pericardial effusion, and the general therapeutic inefficacy of prescribed medications. An electrocardiogram revealed abnormal R–T transitions in all leads.

On September 25, 1933 the patient was observed the third and last time. Several weeks before, he had an attack of tonsillitis followed by fever and fleeting pains in many joints. An outstanding complaint was shortness of breath. On examination a typical generalized erythema marginatum was found on the anterior chest, lower part of the back, left forearm, and posterior aspect of the thighs. The eruption was composed of numerous circular and polycyclic figures showing raised borders and centers colored like chamois skin. There were occasional interspersed discrete papules. Personal observations made over several hours disclosed that definite changes in configuration occurred in many lesions. Physical signs of mitral stenosis, mitral insufficiency, and, perhaps also aortic insufficiency were noted. The liver was palpated 2 cm. below the right costal margin. There was no pretibial edema.

The course was marked by periods of moderate fever, appearance of crops of subcutaneous nodules, and rapid changes in the morphology of the cutaneous lesions. The eruption would come and go in surprising fashion; lesions appearing during the day would vanish overnight, and vice versa. As a rule, the abdomen and chest were the principal areas of involvement, but at times the extremities were also implicated.

On one occasion the fading eruption assumed the features of erythema annulare rheumaticum as a result of flattening of the peripheral margins. In general the onset of the dermatosis was accompanied by signs of rheumatic activity (rise in temperature), but sometimes the lesions would appear in the absence of such evidence. Electrocardiograms disclosed notched QRS complexes and abnormal R–T transitions in all leads. About two weeks before death, the temperature suddenly rose to 103.6° F. Several days later the child complained of pains in the fingers of the right hand; the interphalangeal joints were found to be swollen and tender. Simultaneously, urticarial lesions appeared over the extensor aspects of the thighs and legs, accompanied by puffiness of the eyelids. On the following day the eruption spread over the entire body and assumed a bizarre appearance. On the face (eyes, forehead, chin, and nose) the lesions were erythemato-urticarial in type, arranged in many coalescent patches; on the trunk and extremities there were numerous circles and polycyclic figures, the urticarial component revealing itself as a peripheral white ring of edema when the skin of the affected parts was rendered taut; on the dorsum of the hands there were several erythemato-urticarial lesions arranged in circular configuration. The mucous membranes were spared. There was mild pruritus. A remarkable feature was the constantly changing appearance of the rash. What originally began as an unusual urticarial type of dermatosis now assumed, in the course of 24 hours, the typical morphology of erythema marginatum rheumaticum, with raised red borders and brownish flat centers. On the basis of the extraordinary widespread distribution, involvement of unusual sites as the face and dorsa of the hands, and in the light of a similar case recorded by S. Mackenzie, a fatal issue was prognosticated. The condition of the child became worse; he developed pain in the left wrist; the temperature mounted steadily; epigastric and precordial pain occurred; dyspnea and orthopnea increased in intensity; and the liver became larger. The patient died February 16, 1934.

Postmortem examination revealed universal adherent pericarditis, recent and old mitral valvulitis accompanied by fresh verrucous vegetations on the aortic and tricuspid valves, extensive healed left auricular lesion, bilateral fibrous pleuritis, and generalized serosal hemorrhages (peritoneum, pleurae, and pericardium). Microscopic study showed numerous Aschoff bodies in the heart in various stages of evolution.

Discussion. The tendency for the cutaneous and subcutaneous manifestations of rheumatic fever to reappear in several attacks of the disease is stressed. Of great interest were the remarkable transformations in appearance of the rash as observed several weeks before death.

Case 6. Boy 10 years old; upper respiratory infection, sore throat, fever, pains in joints, urticarial type of erythema marginatum, crops of subcutaneous nodules, electrocardiographic changes; death one year later; postmortem examination: old and fresh rheumatic cardiac disease, with Aschoff bodies in the heart.

A. W., boy aged 10, was seen April 18, 1927. Four weeks before this, he had an upper respiratory infection marked by fever, general malaise, and later by sore throat, pains in the chest, and high fever. A disseminated eruption appeared, covering most of the body excepting the face. The left ankle became swollen and tender to touch. The parents noted that the rash came and went.

On examination physical signs of mitral stenosis and insufficiency were present. The anterior and posterior aspects of the trunk revealed an erythematopapular rash arranged in circinate, gyrate, and irregularly shaped lesions showing dull red margins and fawn-colored centers. The following day subcutaneous nodules appeared on the flexor tendons of the left arm, scalp, each acromial process, and on several of the

vertebral spines. The site of the Pirquet test was, curiously enough, surrounded by an urticarial reaction similar to that observed in some of the cutaneous lesions. Electrocardiograms showed tachycardia and P–R complexes measuring 0.20 sec. The eruption was characterized by transiency of individual lesions. From time to time fresh papules appeared, especially on the back, but within a week the rash had practically faded in its entirety. Several fresh nodules were found on the vertebral spines. At this time electrocardiograms revealed prolonged P–R complexes, measuring up to 0.26 sec. Subsequently, there was a recurrence of the eruption on the trunk. The subcutaneous nodules and cutaneous lesions began to fade. From May 6 to May 11, the temperature was normal, but physical signs appeared to indicate progressive endocardial disease; moreover, fresh nodules continued to present themselves. May 13, a macular erythematous rash appeared on the trunk and thighs, accompanied by a slightly tender subcutaneous nodule on the left fourth finger. The right sterno-clavicular joint was swollen, painful, and tender to touch. Within the next two days the eruption became diffusely distributed, while the sterno-clavicular arthritis subsided. During this period the height of the temperature was 100.6° F.

More than a year later the patient was observed again. Shortly before this, he hiked eight miles, following which he experienced pain in the back of the neck and left side of the chest. He became pale and dyspneic. There was epistaxis. On examination physical signs of mitral stenosis and insufficiency were noted. Evidence of moderate decrease in the cardiac reserve was manifested by a palpable liver and bilateral hydrothorax. Subcutaneous nodules were found about the left elbow and over the first interphalangeal joint of the right middle finger. Electrocardiogram showed prolongation of the P–R complexes. The course was subfebrile. The patient became more "decompensated"; the abdomen and scrotum filled with fluid. There was a leukocytosis (18,300).

Postmortem examination revealed fresh mitral and tricuspid valvulitis and old changes in the mitral valve. The pericardium was also the site of acute and chronic alterations. Bronchopneumonia, petechial hemorrhages scattered throughout the viscera, and the usual evidences of heart failure were the other significant findings. Microscopic studies of the heart showed numerous "myocardial" Aschoff bodies in various stages of evolution.

Case 7. Boy aged 13; previous history of "inflammatory rheumatism" with cardiac involvement; recent recrudescence; fever; tachycardia; leukocytosis; electrocardiographic changes; mitral stenosis and aortic insufficiency; gyrate erythema of rheumatic fever.

P. L., boy aged 13, had, some six years before the present observations, suffered an attack of "inflammatory rheumatism" characterized by pains in the legs and cardiac involvement. The recent illness began several weeks before when he contracted a severe cold accompanied by dyspnea and palpitations. There were frequent attacks of precordial distress. Pretibial edema was not present. A rash had recently appeared on the abdomen.

On examination the abdomen was the site of an eruption composed of many irregularly serpiginous lesions; the primary element was a pinkish papule, fairly circumscribed, ranging in size from 1 to 3 mm. in diameter, and arranged discretely or in coalescent plaques. As the lesions developed, the centers flattened and by coalescence of margins, gyrate figures were formed; the borders of these lesions were slightly raised. Physical signs of mitral stenosis, mitral insufficiency, and aortic insufficiency were noted. Pericardial friction rub was audible. Temperature 102° F.; pulse rate 120. Blood pressure 112 systolic, 0 diastolic. Leukocytosis was pronounced (23,500). Electrocardiographic studies revealed P–R complexes measuring from 0.20 sec. to 0.24 sec., with changes in the QRS complexes in the first and second leads. As the pericardial friction rub became fainter, the physical signs began to

point to probable pericardial effusion, confirmed subsequently by roentgenologic examination. After a subfebrile course of three months, the patient was sent to a hospital devoted to chronic disease.

Case 8. Puerto Rican boy of 9 years; history of an eruption, sore throat, and polyarthritis; on admission: gyrate and marginated erythemas, arthritis, indefinite cardiac signs; crops of gyrate, serpiginous and marginated erythemas; electrocardiographic changes; practically afebrile; follow-up history.

E. L., Puerto Rican boy 9 years old, was seen March 26, 1932. Two months before this, an erythematous rash appeared on the upper parts of the back, with the formation of large patches. The eruption was intensely pruritic (drug or sweat origin?); it was neither raised nor pustular. Various salves were applied without benefit. One month later he complained of pain in the right hip and in the spine; he also had a sore throat. After two weeks the right knee, right ankle, and fourth finger of the left hand became swollen and tender to touch. In the interim the rash increased in extent.

On examination the entire torso was found to be the site of an eruption composed of gyrate and circular lesions. The borders were erythematous and slightly raised above the level of skin; the centers were flat and their color could not be evaluated in view of the normal dark hue of the patient. The right ankle was swollen, red, and tender; the metacarpo-phalangeal joint of the left ring finger was swollen but not red. Except for a faint systolic murmur at the apex of the heart, the cardiac status appeared to be normal. The eruption faded in a few days. April 7, a systolic murmur was audible at the apex of the heart, with transmission to the left axilla. April 11, a fresh crop of cutaneous lesions appeared in the interscapular region and right axilla, the rash fading within the next few days. One week later circular lesions continued to recur over the entire trunk and upper parts of the thighs, only to undergo rapid involution. The lesions varied in size, assumed serpiginous outlines, and cleared centrally as the borders extended centrifugally. An electrocardiogram revealed left axis deviation and abnormal R–T transitions in the first and second leads. An interesting feature was the practically afebrile course, aside from temperature of 101° F. on admission.

Over a year later it was learned that the patient had had occasional attacks of fever. A systolic murmur at the apex of the heart and a suggestive presystolic murmur were noted. The systolic murmur was transmitted to the left axilla.

Discussion. Despite the paucity of clinical evidence, the occurrence of this type of dermatosis, particularly in a child, warranted the diagnosis of rheumatic fever. The eruption was characterized by gyrate, serpiginous, and marginated lesions manifesting favor for the torso, appearing and disappearing rapidly, and recurring in crops. A notable feature was its occurrence on several occasions when the temperature was normal. The association with electrocardiographic changes, articular symptoms, and progressive valvular disease constituted evidence of rheumatic activity. It is possible that the patient was observed during the tail-end of a brief recrudescence of rheumatic fever. The eruption per se probably indicated evidence of continued rheumatic activity, an opinion substantiated by the subsequent rises in temperature while at home. On the basis of the clinical evidence it appears that the course of this case should be labeled as continued and chronic, rather than as an acute exacerbation.

Case 9. Boy of 8; polyarthritis, fever, choreiform movements; first observation: left hemiparesis, vague cardiac signs, afebrile course, erroneous diagnoses of

embolus to the right cerebral hemisphere or neoplasm and, subsequently, of chronic encephalitis; second observation: polyarthritis, pain in chest, gyrate erythema evolving into erythema marginatum, more definite cardiac signs; third observation: erythema marginatum, numerous subcutaneous nodules, mitral stenosis and probably also aortic insufficiency, positive findings by fluoroscopic examination.

I. K., boy 8 years of age, was first seen May 5, 1930. Four months before this he complained of intense pains in the knees and ankles; in rapid succession the elbows and shoulders became involved. The polyarthritis was accompanied by fever reaching a peak of 104° F. A private physician suggested the diagnosis of rheumatic fever. Immediately after the subsidence of the articular pains, choreiform movements developed. Three weeks before, the patient had generalized convulsions, with loss of consciousness. There were no sphincteric disturbances and no biting of the tongue during these attacks. When first observed, there were signs of left hemiparesis accompanied by involvement of the face and tongue and a positive Babinski sign on the affected side. There were constant choreiform movements. He had nine convulsive seizures, with periods of total aphasia and confusion. There were no gross field defects. An indefinite systolic murmur was heard at the apex of the heart. At the end of three weeks the patient was discharged, the condition being diagnosed as embolus to the right hemisphere or neoplasm. Of interest was the afebrile nature of the course. During the next few months there were increasing mental difficulties and peculiarities in behavior, these signs being regarded as evidence favoring the diagnosis of chronic encephalitis.

He was seen a second time April 23, 1931. Four days prior to this observation he suffered from pains in the left chest, knees, elbows, and left thumb. The affected articulations were swollen and tender to touch. On the following day he had fever and became fidgety.

On examination both knees, right elbow, and left hand were swollen, warm, and painful; the affected areas were not red. A rough systolic murmur was audible at the apex of the heart and the pulmonic second sound was accentuated. The liver could just be palpated. On the next day a pale erythematous flat gyrate eruption appeared on the trunk, elbows and thighs. Within 24 hours the lesions extended over the entire glabrous surface of the body, the face excepted. In areas the rash was confluent. Moderate fever persisted. An electrocardiogram revealed occasional auricular extrasystoles and inverted T_3 waves. Within two days the dermatosis assumed a more definitely marginated appearance. The patient complained of pain in the left middle finger. Shortly after, the eruption faded completely. At the time of discharge (May 15) there was a suggestive presystolic murmur at the apex of the heart. A heart sound tracing appeared to indicate the presence of a short diastolic murmur. Several months later a loud systolic murmur was audible at the apex of the heart.

Discussion. It was my belief that this type of dermatosis, occurring in a child, constituted definite evidence of rheumatic fever. Clinically, the cardiac findings were not absolutely typical of valvular disease. Fluoroscopic examination had not been made.

Addendum. I have had the opportunity of observing the child again. The rheumatic etiology of the case is firmly established by the occurrence of erythema marginatum, numerous subcutaneous nodules, and physical signs of mitral stenosis, mitral insufficiency, and aortic insufficiency (?). Electrocardiograms revealed evidence of severe myocardial damage. Fluoroscopic examination showed prominence of the pulmonary conus and definite enlargement of the left auricle with encroachment on the retrocardiac space.

Case 10. Child of 5; previous history of joint pains and fever; spontaneous involution of "ringworm"; pallor; indefinite cardiac signs; subfebrile course; electrocardiogram and sedimentation rate normal; subsequent course: mitral stenosis and aortic insufficiency.

P. G., girl aged 5, was seen May 18, 1932. She had been an inmate of an orphan asylum. For the past year she had joint pains and fever. To alleviate these symptoms the tonsils were removed. During the two weeks preceding this observation, she developed increasing pallor. Temperature was subfebrile. Four days before, an eruption resembling "ringworm" appeared on the left arm; the lesions underwent rapid spontaneous involution.

On examination the child presented marked pallor. No eruption was noted. Physical signs revealed enlargement of the heart to the left, a systolic murmur at the apex, and a booming diastolic murmur in the left third interspace just to the left of the sternum. Roentgenogram showed a cardiac contour suggestive of mitral disease. However, the sedimentation time was over two hours (Linzenmaier method). There were no clinical signs pointing to diminution in cardiac reserve. The course was subfebrile, with intervening period of normal temperature. She was discharged June 13, 1932.

Discussion. The history of spontaneously healing "ringworm" suggested the possibility of a rheumatic origin; this evidence was important in view of the inconclusive data found by clinical and laboratory examinations. This opinion was substantiated by the subsequent course.

Addendum. In a recent communication from her attending physician, it was learned that the child had undoubted evidence of rheumatic heart disease. There were physical signs of mitral stenosis and aortic insufficiency, the murmurs showing tendency to vary in quality from time to time. There was now a definite Corrigan pulse. She suffered occasional attacks of fever and increasing pallor.

Case 11. Puerto Rican man of 26; two previous attacks of rheumatic fever; recent polyarthritis; sudden onset of aphonia; urticarial type of erythema marginatum; aortic insufficiency; fusiform fingers; pains in right hip and neck; fever; electrocardiographic changes; epistaxis; second crop of cutaneous lesions.

R. N., Puerto Rican man 26 years old, had an attack of acute rheumatism with cardiac involvement in 1921. Several years later there was a recrudescence. Three months before the present observation, he complained of pain in several joints, but these were neither red nor swollen. About two months later he had a sudden attack of aphonia and could barely speak in a whisper. There had been no antecedent sore throat.

On examination the torso was found to be the site of a generalized eruption composed of erythematous lesions situated on the right side of the neck and erythematopapular efflorescences on the abdomen and back, forming small coin-sized circular configurations. Physical signs of aortic insufficiency were noted. The terminal joints of the fingers, excepting those of the thumb, were fusiform in shape. He complained of stiffness and pain on flexion of the neck. The right hip was also painful on active and passive motion. Temperature was 102° F. There was moderate leukocytosis. Blood pressure was 145 systolic, 0 diastolic. On the next day there was a sudden onset of auricular fibrillation, and, about 20 hours later, a fresh crop of erythematopapular lesions appeared on the trunk. Three days after the onset of auricular fibrillation, the pulse became regular again. An electrocardiogram

revealed left axis deviation and prolonged P–R complexes (0.24 sec.). After a short stay the patient was sent home.

Case 12. Boy of 10; previous history of heart disease (?) and vague muscle and articular pains; recent illness: abdominal pain, tonsillitis, "grippe," epistaxis, swollen painful knee; crops of annular erythema; no definite cardiac abnormalities, one normal electrocardiogram.

J. D., boy aged 10, was seen March 8, 1933. Following bilateral mastoidectomy in 1926, a private physician suggested that the boy had rheumatic heart disease, the diagnosis being based on the presence of a cardiac murmur. At no time had there been rheumatic stigmas, except for occasional complaints of vague muscle and articular pains. Three years later the cardiac murmur was no longer audible. Six weeks before the present observation, he had abdominal pain in the right side of the abdomen, the condition subsiding spontaneously in a short time. Subsequently, he had an attack of tonsillitis and "grippe" associated with vague pains in the abdomen, chest, and legs. This was followed by epistaxis. The temperature rose to 102° F. The left knee became swollen and painful.

On examination the skin was pale and sallow. There were enlarged tender submaxillary glands with evidence of tonsillitis and pharyngitis. A short soft localized systolic murmur was heard at the apex of the heart. A moderately loud systolic murmur was also audible at the aortic area of the heart. Temperature was 102° F.; pulse rate 88. March 10, salicylate therapy was started. On the following day the patient was afebrile. There were dull red, flat, discrete, annular lesions with pale yellow centers, the eruption involving both forearms and legs. The lesions disappeared spontaneously in a few hours, but recurred on the succeeding day. Sedimentation time was 40 minutes. The white blood cell count was 8,000 with 73 per cent polymorphonuclear leukocytes. An electrocardiogram disclosed no abnormalities. March 13, the sedimentation time was 16 minutes; the eruption had practically faded; and no cardiac murmurs were audible. Subsequently, similarly configurated lesions appeared on the lower part of the abdomen, the rash being characterized by the rapidity with which it faded from one area and reappeared in another. Finally, the joint pains subsided and the patient was discharged. The case was regarded as one of rheumatic fever.

It was learned, several weeks later, that articular pains had recurred. Examination of the heart showed no abnormalities.

Discussion. In the absence of positive evidence of valvulitis or of myocardial damage (only one electrocardiogram taken), the diagnosis of rheumatic fever may be viewed with reserve. The morphology and ephemeral nature of the cutaneous lesions recalled the type of eruption that is generally encountered in this disease. The numerous sore throats, transient involvement of articulations in a child, onset with epistaxis, and the peculiar dermatosis favored the rheumatic etiology of this particular case. In the succeeding instances to be detailed the evidence for the diagnosis of rheumatic fever will be found to be more conclusive.

Case 13. Girl of 11 years; previous upper respiratory infection and cardiac murmur; pains in legs; fever; flat annular erythema; indefinite signs of mitral disease; joint pains; disappearance of cardiac murmurs; subsequent attacks of acute rheumatic fever with heart failure.

R. S., girl 11 years old, was first seen March 26, 1930. In 1929 she had an upper respiratory infection and at this time a cardiac murmur was heard. Three months before the present observation she experienced pain in the legs; the temperature rose

to 104° F. This febrile condition continued for one month; she was permitted to walk about, but illness forced her to return to bed.

On examination the abdomen and chest were sites of erythematous polycyclic configurated patches that faded by the following day. A systolic murmur was heard in the left fourth intercostal space. The pulmonic second sound was louder than the aortic second sound, but not accentuated. Temperature was 102° F.; pulse rate 112. An electrocardiogram showed only right axis deviation. Subsequently, she complained of pains in the arms and legs, and a blotchy erythema appeared on the trunk. Within several hours the eruption disappeared, leaving a few tiny patches colored dark brown. A systolic murmur was heard at the apex of the heart; it was transmitted to the left axilla. She complained of slight pain in the wrist, index fingers, right shoulder, and right hip, the affected joints being neither red nor swollen. Temperature was 101° F.; pulse rate 112. At the time of discharge the cardiac murmurs were no longer audible. The course had been subfebrile. The case was classified as a probable instance of acute rheumatic fever.

Discussion. The type of eruption appeared to substantiate the diagnosis of rheumatic fever, this belief being confirmed by the subsequent course.

Addendum. The patient was seen again September, 1930; examination of the heart disclosed no abnormalities. She was observed again in January, 1932; in the interim she had suffered from several attacks of acute rheumatic fever accompanied by cardiac involvement and the usual evidence of myocardial (congestive) failure. The importance of an adequate follow-up is illustrated by this case.

Case 14. Child of 10; tonsillectomy; bronchopneumonia; systolic murmur at the apex of the heart; recent illness: fever, ringed eruption on forearms, flat annular erythema, development of definite signs of mitral stenosis, pain in one shoulder, two normal electrocardiograms.

R. B., girl 10 years old, was observed April 3, 1933. In 1925 the tonsils and adenoids were removed for the alleviation of repeated sore throats. Three years later she had an attack of bronchopneumonia; examination of the heart revealed no abnormalities at this time, aside from a systolic murmur localized to the apex. However, one year later a private physician discovered a cardiac murmur which he considered as significant (no details available). The recent illness dated back three weeks, when she experienced sensations of chilliness. Temperature was 104° F. About a week before the present observation her mother noticed a ring-like eruption on the forearms, the lesions disappearing by the following day.

On examination a faint systolic murmur was audible at the apex of the heart. Percussion revealed that the cardiac outlines were enlarged to the right and left. Temperature was 101.5° F.; pulse rate 120. Moderate leukocytosis was present. The diagnosis of rheumatic fever was suggested. Roentgenogram of the chest revealed enlargement of the left ventricle and prominent pulmonary conus, suggesting involvement of the mitral valve. During the following week the temperature was subfebrile. At the end of this period the temperature became normal and a faint pinkish, barely discernible annular rash appeared on the chest. Within a few hours the lesions underwent complete involution. Two days later a presystolic rumble was heard at the apex of the heart, accompanied by a roughened first sound. After an afebrile period of two weeks, the temperature rose to 101° F. and the patient complained of pain in the left shoulder. Salicylate therapy was effective in controlling the articular symptoms. Two electrocardiograms disclosed no significant abnormalities.

Discussion. The presence of this ephemeral eruption appeared to corroborate the diagnosis of rheumatic fever, even in the absence of electrocardiographic changes. It is interesting that the lesions appeared during an afebrile period, only to be succeeded by pain in the shoulder and fever. The previous history of a ringed eruption is stressed.

Case 15. Child of 12; previous attack of chorea; tonsillectomy; vague fleeting pains; present illness: fever, precordial pain, abdominal cramps, flat annular erythema, electrocardiographic changes.

M. S., girl of 12 years, was seen in 1929. At the age of 8 she had a mild attack of chorea. Because the child suffered from frequent sore throats, the tonsils were removed. Two years before the present observation, she had an upper respiratory infection, with pains in the muscles and bones; a cardiac murmur was heard at this time. Since then, she occasionally complained of fleeting articular and muscle pains. Two weeks prior to hospitalization she had a "cold," characterized by general malaise and fever up to 102° F. She experienced stabbing pains in the precordial region. A rash appeared on the right arm, spreading rapidly over the entire torso. Several days later she complained of severe abdominal pains and vomited once. Temperature was 104° F.

On examination physical signs of mitral stenosis and aortic insufficiency were noted. Temperature was 103° F.; pulse rate 112. There were numerous dull red circular lesions on the upper extremities, particularly on the dorsal aspects of the forearms. These varied in diameter from 2 to 10 mm. and apparently showed clear centers. A similar eruption was observed on the anterior and posterior aspects of the trunk. The largest lesions were found on the upper part of the abdomen where they were irregularly circular, with fawn-colored centers. There was a marked leukocytosis (20,400). Electrocardiographic tracings revealed P–R complexes measuring from 0.22 sec. to 0.24 sec., with flat T-waves in the first lead. The temperature gradually fell to normal. By the third day of observation the eruption had practically faded. The remainder of the course was uneventful.

Case 16. Boy of 17; previous history of pain in the knees; recent illness: abdominal pain, diarrhea, fever, vague arthralgias; probable mitral stenosis; flat annular erythema; electrocardiographic changes; fluoroscopic examination: enlarged left auricle and ventricle.

M. J., boy aged 17, was observed April 19, 1932. Two years before this, he was confined to bed because of pain in the knees, the illness being considered as of rheumatic origin. His recent illness dated back one week when he complained of headache, discomfort in the umbilical region, nausea, and vomiting. On the next day the abdominal pains became continuous. There were several attacks of diarrhea, accompanied by fever. He noted pains in the bend of the right elbow and below both knees, but the affected areas were neither red nor swollen. When first seen, the chief complaints were those of persistent diarrhea and para-umbilical pain.

On examination a short blowing systolic murmur was heard at the apex of the heart; the rhythm was tripartite. The pulmonic second sound was slightly accentuated. The edge of the spleen was palpated one finger's breadth below the left costal margin. Temperature was 101.6° F.; the pulse rate 100. There were two irregularly circinate lesions on the lateral aspects of the right antecubital space, each about one cm. in diameter, with distinct red flat borders and pale yellow centers. There was no leukocytosis (8,800). It was generally believed that the case was one of rheumatic fever. The eruption was classified as erythema annulare rheumaticum, an opinion strengthened by spontaneous involution of lesions overnight. There was

disagreement with this view inasmuch as the temperature fell to normal in two days with maintenance of that level for the remainder of the course; the eruption was not considered significant by some observers, particularly those who saw the patient after the disappearance of the lesions. With the assumption of a slower cardiac rate several days later, a typical presystolic crescendo murmur was heard at the apex of the heart. Electrocardiographic tracings now showed prolongation of the P–R complexes (0.21 sec. to 0.24 sec.), with inversion of the P-waves in the second and third leads. Fluoroscopic examination disclosed enlargement of the left auricle and ventricle. Subsequently, the spleen diminished in size until it could no longer be palpated. At the end of the course the patient was asymptomatic; an electrocardiogram normal; and sedimentation time 43 minutes.

Discussion. The diagnosis of rheumatic fever in this mild atypical example of the disease was materially aided by knowledge of the cutaneous manifestations. This opinion was subsequently substantiated by clinical and laboratory findings. The transiency of the lesions was a striking feature, serving to strengthen the belief in its rheumatic origin.

Case 17. Boy of 12; several attacks of rheumatic fever; subcutaneous nodules; heart failure; flat annular erythema associated with myocardial failure; postmortem examination: acute and chronic rheumatic heart disease.

S. M., boy aged 12, was first seen December 25, 1928. Three months before this, his tonsils were removed. His recent illness dated back six days when he had an attack of swollen, painful joints, fever, and precordial pain. On examination physical signs of mitral stenosis, mitral insufficiency, pericarditis, pulmonary congestion, and hepatic enlargement were noted. Under salicylate therapy and rest in bed for seven weeks, he improved sufficiently to be sent home.

He was seen again in 1929. During a stay of several months he suffered from a typical recrudescence of rheumatic fever, characterized by polyarthralgias, fever, progressive anemia, repeated epistaxis, and crops of subcutaneous nodules. In addition to the mitral lesion, there were now physical signs of aortic insufficiency.

In 1930 the patient was observed in a state of congestive failure (edema of the ankles, ascites, fluid in the pleural and pericardial cavities, hepatomegaly). He recovered from this attack.

He was observed a fourth time May 2, 1931. There was evidence of progressive diminution in cardiac reserve. Temperature was 101° F.; pulse rate 116. Leukocytosis was moderate (13,000). A scattered eruption composed of violaceous, flat, circular lesions, each about 0.7 cm. in diameter, was seen on the chest and abdomen; the lesions faded on pressure. There were no subjective symptoms referable to the dermatosis which, moreover, disappeared in a few days. After a subfebrile course of one week, the patient was sent to a hospital devoted to the care of chronic disease.

Addendum. The patient died at an institution some two years later. There were clinical signs of progressive heart failure and evidence of rheumatic activity. Necropsy examination disclosed old and fresh rheumatic lesions of all the valves of the heart, with adherent pericardium.

Note: The observations reported in this paper were made in the services of Drs. B. Schick, B. S. Oppenheimer and the late L. Gross, and I am also indebted to them for perusal of the original manuscript containing these data.

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CASE REPORTS

CONGENITAL HEART BLOCK; REPORT OF A CASE OF SUSPECTED INTERVENTRICULAR SEPTAL DEFECT (MALADIE DE ROGER) WITH COMPLETE HEART BLOCK*

By CLARENCE D. MOLL, M.D., F.A.C.P., *Detroit, Michigan*

FOR clinical purposes congenital lesions of the heart may be divided into two groups: (1) those showing cyanosis as a conspicuous feature, and (2) those without cyanosis except as a transient or terminal event. Diagnosis of cases of the first group is rarely missed; in those of the second group, however, failure of diagnosis occurs with greater frequency. Certain congenital cardiac lesions are incompatible with more than a brief span of life and these have only a passing academic interest for the clinician for he rarely sees them. On the other hand there are those that cause slight or no disability to the patient except when some other condition supervenes to aggravate the heart status.

Maude E. Abbott, who has written extensively on congenital cardiac lesions and to whom we are indebted for clarification of this subject, has analyzed over 1,000 cases with autopsy findings. From this extensive survey we can gain some idea of the relative frequency of the different lesions. This study indicated that the following were found most often: Patent foramen ovale, defects of the interventricular septum, patent ductus arteriosus, coarctation of the aorta, pulmonary stenosis, and anomalies of the semilunar cusps. All other defects were less common.

In the case of ventricular septal defects the size of the aperture may vary greatly; there may even be complete absence of the septum. The presence of the defect is usually marked by a harsh systolic murmur with maximum intensity over the precordium to the left of the sternum in the second or third interspaces. It may be accompanied by a thrill in this area. Transmission is usually in all directions and occasionally to the back. The loudness of the murmur varies inversely with the size of the opening, thus the smallest openings give the loudest murmurs. Absence of symptoms with such distinctive signs is characteristic of these lesions and cyanosis is rarely present except as a terminal feature. Normally the intraventricular pressure is greater in the left side of the heart than in the right and the flow of blood through the opening therefore is from left to right. However, any condition which would raise the pressure in the right ventricle over that in the left would reverse the blood flow and venous blood would mix freely with arterial in the left chamber and produce cyanosis in the peripheral circulation. Increase in the blood pressure in the pulmonary circuit may be produced by some of the common lung conditions such as pneumonia, bronchitis, emphysema, etc., or by tumors of the mediastinum.

Defects at the base of the interventricular septum sometimes interfere with

* Received for publication March 29, 1937.

the continuity of the conduction tissue leading to bundle branch block or complete heart block. As commonly as this particular phenomenon might be expected to occur Abbott reports only 16 cases in her series. In 1928 Yater had reviewed the literature to date and found only 29 cases of congenital heart block which he considered sufficiently proved to be considered as such. He added one of his own and outlined certain criteria which he considered essential to such a diagnosis. After the presence of heart block has been established by graphic methods it is necessary to differentiate whether the condition is congenital or acquired. There must be some evidence of a slow pulse at an early age and absence of a history of any infection which might cause the condition after birth: notably, diphtheria, rheumatic fever, chorea or congenital syphilis. The occurrence of syncopal attacks in early life is fairly good evidence of the existence of the heart block prior to the attacks. The presence of signs of congenital heart disease, although not essential, adds weight to the diagnosis of a congenital origin of the condition.

With this brief general discussion I would like to present the following case history which, I feel, fairly well fulfills the above criteria for the diagnosis of congenital heart block as a result of a defect at the base of the interventricular septum.

Case Report

Miss E. M., 18 years of age, a high-school student, came under observation because she had been told at school by the doctor that she had heart trouble and had

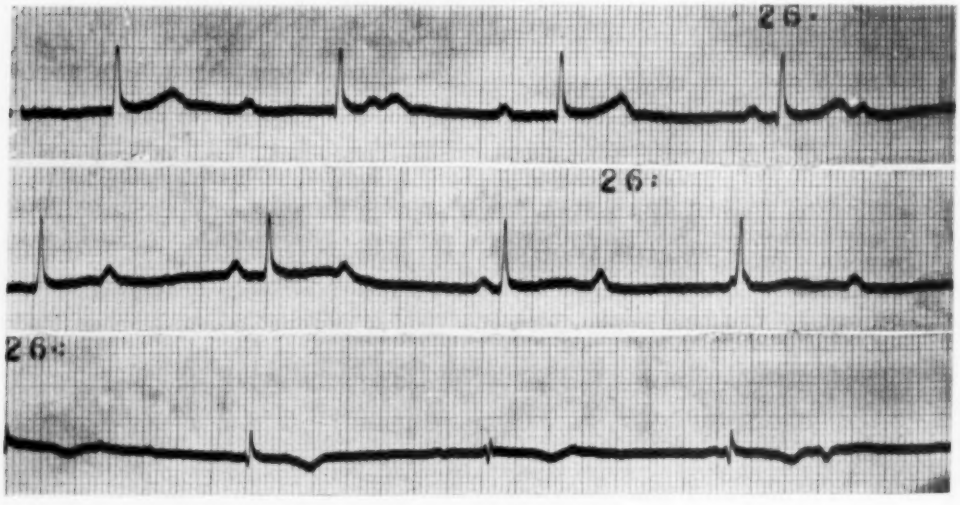

Fig. 1. Complete heart block. Rate of auricles 75 and of ventricles 41. Leads I, II, and III in order from above downward.

been forbidden to take "gym" work. She was not complaining of any marked symptoms referable to her heart but on questioning her I found that she had been told when she first entered school at the age of six years, that she had a very slow pulse and a large heart. She had, however, been able to play all the games and engage in the activities that girls ordinarily do. She did admit that for the past

2½ years she had noticed that she "winded" more easily upon exertion. There had never been any history of rheumatic fever, chorea, growing pains or frequent sore throats. No cyanosis had ever been present.

Physical examination showed her to be well developed and nourished, with good color, and no apparent difficulty in breathing. Her fingers and toes showed no cyanosis or clubbing. The examination, other than of the heart, was essentially negative. The cardiac apex beat was felt in the fifth interspace 7 cm. from the midsternal line. Over a small area just to the left of the sternum in the fourth interspace there was a slight thrill. The sounds were regular and of good quality but the rate was very slow—41 per minute. From the second to the fourth interspace along the left sternal border there was heard a harsh systolic murmur. This was transmitted in all directions but not to the back nor to the neck vessels. Blood pressure was 110 systolic and 60 diastolic. The Kahn test was negative. Fluoroscopic examination of the thorax showed slight enlargement in the transverse cardiac diameter, both ventricles being equally affected. The great vessel contour was normal. The electrocardiogram (figure 1) disclosed a complete heart block with total dissociation of auricular and ventricular rate; auricular rate 75 and ventricular 41.

DISCUSSION AND CONCLUSION

Thus we are dealing with a complete heart block in this case at an early age when such a finding is rather unusual. In the absence of a history of an infection such as rheumatic fever, chorea, frequent sore throats, or congenital syphilis such a condition would lead one to postulate the possibility of congenital origin. This is further enhanced in this case by the history that this patient had been told at the age of six years that she had a very slow pulse. In view of the physical signs it is felt that the continuity of the Bundle of His was interrupted by a defect in the interventricular septum at the base.

These cases usually carry on for many years unhampered by their defect. However, a large number eventually develop a bacterial endocarditis or Stokes-Adams attacks. Abbott reports that 41 per cent of her cases developed subacute bacterial endocarditis as a terminal complication.

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POSTOPERATIVE PULMONARY ATELECTASIS; REPORT OF A CASE TREATED BY ARTIFICIAL PNEUMOTHORAX*

By JOHN A. SCHINDLER, M.A., M.D., and W. B. GNAGI, JR., B.A., M.D.,
Monroe, Wisconsin

POSTOPERATIVE atelectasis or massive pulmonary collapse of sufficient degree to cause aggravating symptoms is not infrequent. In Brunn and Brill's [1] series of 456 abdominal operations the incidence of postoperative atelectasis was 4.8 per cent, and in Snyder's [2] series of 630 abdominal operations the incidence was 1.6 per cent. Lesser degrees of atelectasis causing so little respiratory and circulatory distress as to escape casual notice occur much more frequently, and can be detected only by postoperative chest roentgenograms.

As a rule postoperative collapse runs a benign non-fatal course and its occurrence usually need arouse but little trepidation. In a small percentage, however, the atelectasis may end fatally with the signs and symptoms of pneumonia; and in still other cases which ultimately recover the onset and course of the collapse may be attended by such extremely distressing symptoms that one fears for the safety of the patient. From two cases which have come to autopsy and from a careful clinical study of 10 others, it may be suggested that:

(1) The distress of the patient is proportional to the area of atelectatic lung. The more extensive the atelectasis the greater the mediastinal shift. The resulting distress is probably due not so much to traction on the trachea as to traction on the large vessels.

(2) The severity of the disease is furthermore affected by the secondary occurrence of a pneumonia in the atelectatic lung. That this occurs has been questioned by some, notably Churchill,[3] but has been verified by Lee, Tucker and Clerf,[4] Coryllos and Birnbaum,[5] and Lubin.[6]

(3) The severity of the disease is further affected by the type of organism producing the secondary pneumonia. By sputum studies in our cases it is apparent that the majority of infections are produced by the types of pneumococci which are often found in throats of normal individuals. These types produce the less severe pneumococcus pneumonias. However, in the fatal or toxic cases the organism is more apt to be types III, II, or I, which are less often found in the normal throat. We view with alarm a case of atelectasis where the early sputum specimens (which can be secured in most cases) show a type III pneumococcus. The cases with types I and II can be benefited with anti-pneumococcic serum. In type III infections we are of course without this help.

In the case we are reporting the clinical picture was that of a highly toxic and severe infection aggravated by the distress of a marked mediastinal shift. The roentgenograms indicated atelectasis in an entire lobe, while the early sputum, and the mucous plug later expectorated, showed a type III pneumococcus. This in our experience is a type of atelectasis with a grave prognosis.

The specific measures which have been devised for the treatment of atelectasis are few in number. The most readily available is Sante's [7] method of rapidly turning the patient from side to side in an effort to dislodge the obstructing mucous plug. Another is the use of 5 per cent carbon dioxide inhalations to

* Received for publication June 27, 1937.

increase the respiratory depth and so forcibly dislodge the plug. These two methods we have often found to fail as they did in the present reported case. More effective, but much more heroic and accompanied by more discomfort to the patient, is the use of bronchoscopy in aspirating the bronchial plug, first utilized by Jackson and Lee [8] in 1925.

The use of pneumothorax in the present case was suggested by our practice in the past three years of treating all Type III pneumococcus pneumonias by artificial pneumothorax. Types I, II, V and VII we have treated serologically. The appearance of a Type III infection in a postoperative atelectasis immediately suggested artificial pneumothorax as a treatment. *A priori* reasoning lent further plausibility to the method on the following grounds:

(1) Air placed in the pleural cavity on the affected side could be expected to push the mediastinum back into its original position and thus immediately relieve the distress attendant upon the tracheal and large vessel displacement.

(2) The pneumothorax might be expected to dislodge the bronchial plug by pressure. In any case it might be expected to influence the severity of the Type III infection in the atelectatic lung just as it has in our cases of Type III lobar pneumonia.

These expectations were borne out in a dramatic fashion as the case report shows.

A review of the literature revealed reports of several other cases of atelectasis treated by pneumothorax. As early as 1914 Elliott and Dingley [9] wrote, without reporting any cases, "It is conceivable that intrapleural injection of oxygen, in order to restore balance of volume and push back the displaced heart and lung, might relieve the worst cases of cyanosis and dyspnea."

In 1928 Habliston [10] reported four cases of atelectasis, two occurring in pulmonary tuberculosis, one from thoracic aneurysm, and one following a crushing injury to the thigh, treated by pneumothorax. Ashbury [11] in 1929 resorted to artificial pneumothorax in an atelectasis resulting from a benign intrabronchial tumor. In this case the tumor was forcibly expectorated when the collapse was being completed. In 1930 Moorman [12] used artificial pneumothorax in an atelectasis which developed two days after an appendectomy. In each of these reported cases the pneumothorax was quickly followed with relief of symptoms. Noveau [13] reported its successful use in atelectasis accompanying tuberculosis.

Case Report

December 26, 1935: Mary L. W., aged 12, white, weighing 78 pounds, was admitted to the Deaconess Hospital at 8 p.m. For the 12 hours previous to admission she had suffered an increasingly severe pain in the right lower quadrant and had vomited several times. There were well marked tenderness and rigidity over McBurney's area. The upper respiratory tract and chest were entirely negative. The temperature was 100.2° F. orally. The white cell count was 12,500 with the Schilling revealing a marked shift to the left. The urine was negative. At 9 p.m. an operation was performed and an acute suppurative appendix removed in the usual manner.

December 27, 1935: On the morning following operation the patient's temperature was 99° orally, pulse 90, and respiration 20 per minute. Her condition seemed satisfactory. But during the day and following night the temperature, pulse, and respiration gradually increased.

December 28, 1935: The following morning the patient's temperature was 103° F. orally, the pulse 130 and the respiration 40 per minute. The white blood count was

21,600. She appeared alarmingly ill and distressingly uncomfortable as she fought with an aggravating dyspnea. The marked cyanosis became deeper during the spells of spasmodic and paroxysmal coughing, during which she cried with pain and struggled for the next breath.

Excursion of the chest was greatly limited on the right. The trachea could be felt to have deviated sharply to the right, and the apex impulse was palpated just barely to the left of the sternum in the fifth interspace. The percussion note over the middle and upper right chest was impaired, and the breath sounds were hardly audible. The abdomen was negative except for the recent abdominal incision.

A roentgenogram (figure 1) taken at noon (December 28) showed a marked

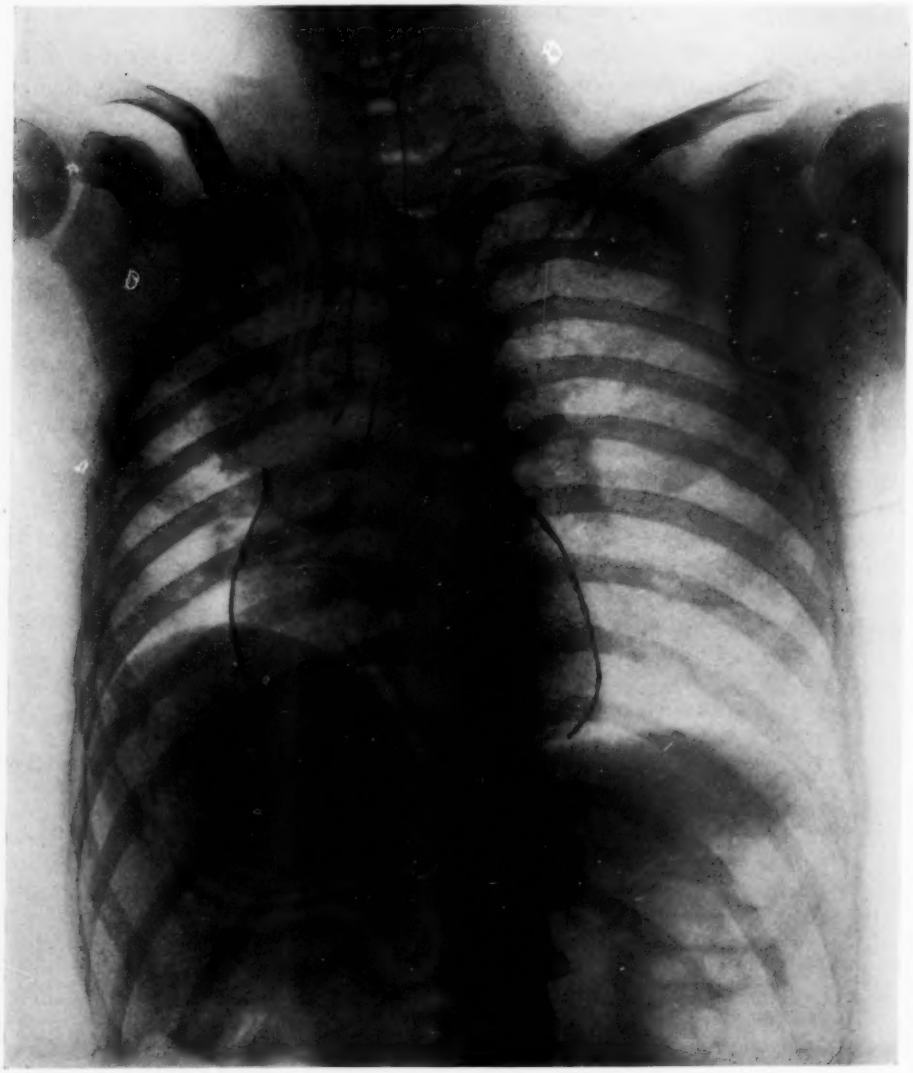

FIG. 1. Roentgenograph taken at noon, December 28, showing a marked deviation of the trachea and heart to the right, elevation of the right diaphragm and a shadow of increased density in the upper right lung field. Temperature 103° F., pulse 130, respiration 40.

deviation of the trachea to the right, a shift of the heart shadow to the right, elevation of the right leaf of the diaphragm, narrowing of the right intercostal spaces, and a broad triangular shadow of increased density spreading from the upper right hilum out over the upper and middle right lung fields.

The small amounts of sputum which the patient could be induced to expectorate with the cough showed a Type III pneumococcus when typed by the Neufeld method. This was checked by mouse peritoneal injection of a portion of the mucous plug described below, in which Type III pneumococcus was again found.

Sante's postural treatment was tried but the manipulation produced so much pain in the region of the incision that it had to be discontinued. Inhalation of 5 per cent carbon dioxide merely served to increase the patient's discomfort.

At one p.m. (December 28) a right artificial pneumothorax was done. The intrapleural pressure on the right was — 150 mm. of water before air was introduced. The pressure in the left intrapleural space was — 65 mm. of water during expiration. Air was allowed to enter the right pleural cavity at the rate of 40 c.c. per minute.

When 300 c.c. of air had been introduced the patient suddenly coughed violently, expectorating with practically the first cough, lumps of tenacious, viscid, yellow-green sputum, one lump in particular being almost cherry sized. The pneumothorax was stopped. At 5 p.m. the same afternoon, 325 c.c. of air were injected into the right pleural cavity. Further injection was again stopped because of cough, which however, was much less severe and raised only a small amount of yellow-green sputum, this time not so viscid. The intrapleural pressure was left at a mean of + 10 mm. of water.

An hour after the second pneumothorax the patient felt much better. Breathing was easier and slower. By five o'clock the next morning, or 12 hours later, the temperature had dropped to 99.6°, the respiration to 20, and the pulse to 102. She had an appearance no different from any other fourth postoperative day appendectomy patient.

At 10 a.m. (December 29), 275 c.c. of additional air were injected into the right pleural cavity, this time without any coughing, bringing the mean intrapleural pressure to + 20 mm. of water. Following this injection a roentgenogram (figure 2) showed a good collapse of the right lung, the greatest amount of collapse being in the involved upper lobe; the mediastinum, trachea and heart had resumed their normal position.

From this time the temperature never rose above 100° F. On the seventh postoperative day (fourth postpneumothorax day) she was allowed to sit up in bed; on the ninth postoperative she sat up and on the tenth day she was discharged. There was only a slight cough, no dyspnea whatsoever.

The total amount of air injected was 900 c.c.

A month later the patient was fluoroscoped. The lung had fully reëxpanded and had resumed a normal appearance.

Discussion

A point of passing interest is the low intrapleural pressure secured on the side of the atelectasis, namely — 150 mm. of water (expiratory) and a pressure of — 65 mm. (expiratory) in the opposite pleural cavity. Coryllos and Birnbaum [14] found that the normal intrapleural pressure averaged — 40 mm. in water in expiration and — 70 mm. of water in inspiration. Elkin [15] found the intrapleural pressures in normal individuals to have similar values, — 9 mm. of mercury in inspiration and — 7 mm. during expiration. Elkin,[15] Habliston [10]

and Coryllos and Birnbaum [14] found practically normal pressures on the uninvolved side in atelectasis, and markedly increased negative pressures on the involved side which sometimes measured as low as —337 mm. of water (Habliston).

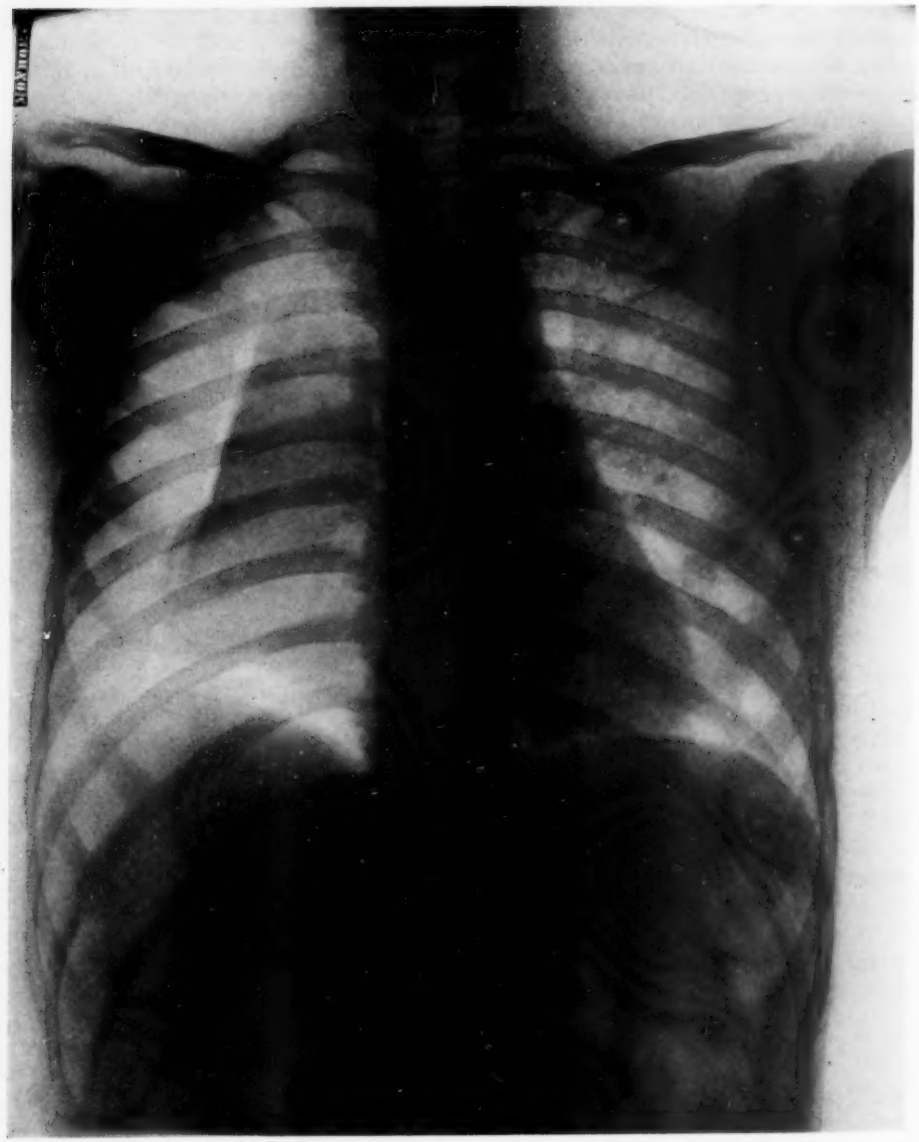

FIG. 2. Roentgenogram taken at noon, December 29, after three intrapleural injections of air totalling 900 c.c. The trachea, heart and right diaphragm have resumed their normal position, and there is a good collapse of the involved lung. Temperature 99.8° F., pulse 104, respiration 20.

A major question may be raised concerning the possibility, and further, the benefit of compressing the already collapsed atelectatic lung. It must be remembered that the volume of the atelectatic lung decreases as the gas within it is absorbed, but the extent of the decrease will be determined by the gas tension of the blood, below which absorption will not take place, and by the elasticity of the structures which are available to occupy the space of the absorbed gas. As the latter factor is definitely limited, the atelectatic lung will be held in partial expansion by the negative pressure within the pleura. That the atelectatic lung is not completely collapsed is plainly evidenced by the further marked decrease in its volume, shown in the roentgenograms, as the pneumothorax has been completed.

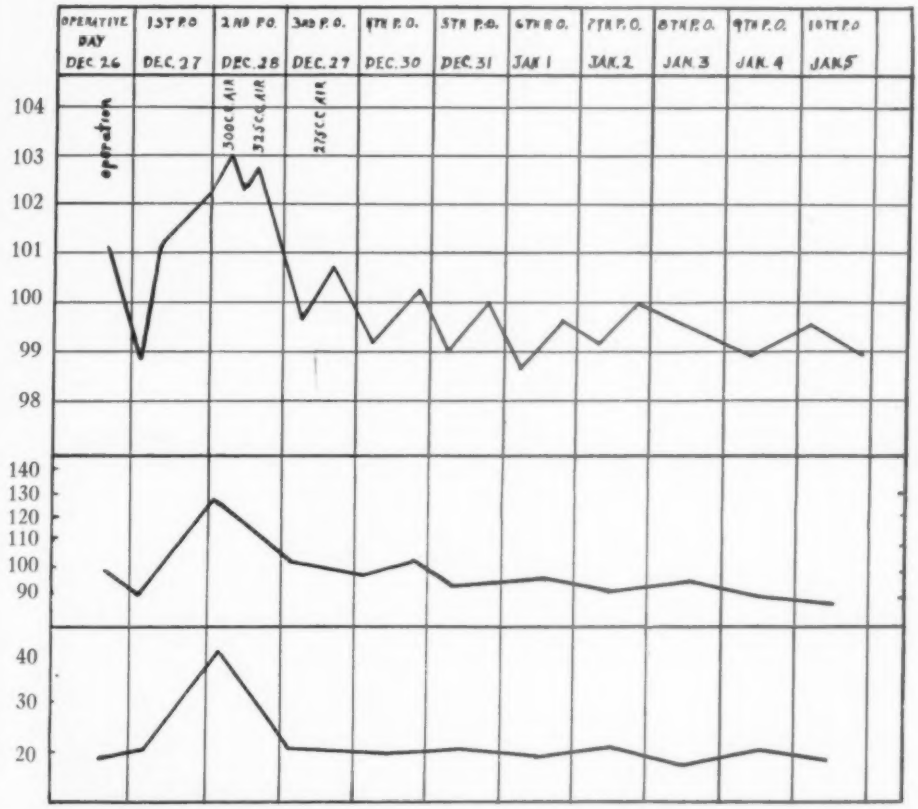

FIG. 3. Temperature, pulse and respiration of the patient during the entire hospital stay.

As in the similar treatment of pneumonia, the following possible explanations for favorable results may be suggested:

(1) The pneumothorax effectively places the diseased lung at rest. On fluoroscopy it will be seen that the movement of the lung on the side of artificial pneumothorax is very slight.

(2) Completing the collapse of the involved lung reduces the in vivo culture tube (the lung) to a fraction of its former size. Bacterial multiplication and toxin production are thereby limited proportionally.

(3) The completion of the collapse greatly reduces the volume of blood flow through the lung, thus limiting at once the toxin absorption and the amount of non-oxygenated hemoglobin returned into the arterial system. This latter results in the immediate reduction of cyanosis, which is so strikingly evident in the collapse therapy of pneumonia.

For a time the evidence of Cloetta,[16] Anderes,[17] and Sauerbruck,[18] tended to show that an increase in the volume of blood flow occurred in atelectasis. However, in the past 25 years indisputable evidence has been presented by Bruns,[19] Weber,[20] Propping,[21] Yates,[22] Coryllos and Birnbaum,[5] Moore,[23] Fine and Drinker,[24] and May,[25] that the volume and velocity of blood flow are markedly reduced in lung collapse. Fine and Drinker [24] have shown that in atelectasis the blood flow through the affected lung is decreased on the average by 46.9 per cent. The volume of blood flow, they showed, is further decreased by as much as 82 per cent by additional compression to secure a complete collapse.

Conclusion

Although usually a condition without grave danger, postoperative atelectasis may at times present so alarming a picture that one would welcome an effective method of treatment. This is usually true when three factors intervene: a large area of atelectasis, a pneumonic process engrafted on the atelectatic area, and a virulent organism producing the pneumonia. In such a condition artificial pneumothorax is a rational procedure, and as a few instances in the literature and one case suggest, may be a highly effective one.

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EDITORIAL

PROTHROMBIN DEFICIENCY IN RELATION TO THE BLEEDING TENDENCY

THE essential step in blood coagulation is the change of a soluble protein-like substance, fibrinogen, to an insoluble gel called fibrin. This gel is normally rapidly formed when blood is extravasated; and under certain circumstances it may be formed intravascularly. The clotting of extravasated blood is the most important defense against undue hemorrhage. If there is a high grade defect of coagulation the patient will exhibit a bleeding tendency. The nature of such defects in the mechanism of coagulation is, therefore, a subject of intense clinical interest.

The theories of blood coagulation are notoriously complicated and unsatisfactory. There is, however, general agreement that fibrinogen will not change to fibrin unless the solution contain adequate amounts of three other substances: (1) a substance normally present in plasma termed prothrombin, (2) a certain amount of calcium, (3) and a substance derivable either from platelets or from certain tissues, often called thromboplastin. The interaction of these three is supposed to alter prothrombin to thrombin and the latter then acts upon fibrinogen and changes it to fibrin. It is also postulated by some that an anticoagulant which inhibits this reaction is present in circulating blood and accounts for the absence under normal conditions of intravascular clots. Howell termed it "heparin." With all of these factors present, it is obvious that the theoretical possibilities as to the nature of a defect in coagulation are almost unlimited. It is only as undisputed experimental facts accumulate that we are able to set aside, as ruled out by the evidence, an increasing number of such theories.

Among the clinical types of bleeding which have been most puzzling are those often fatal cases associated with obstruction of the bile passages, those seen in severe liver injury, and those that develop in certain cases with persistent biliary fistulae. In all of these conditions, spontaneous bleeding into the skin, from mucous membranes, from the kidneys and into the body cavities, may occur; or bleeding may appear during or after operation from the drainage tubes, or into or about the viscera involved. The nature of the defect in blood coagulation in these cases has been extremely obscure until recent work appeared which promises to throw some light upon the process.

Previous studies have shown that samples of blood from such cases might show normal coagulation time, a normal type of clot, a normal number of platelets, a normal content of calcium and of fibrinogen and yet after operation the patient might bleed fatally. These factors were the only ones measurable until recently. A quantitative measure of prothrombin was not available.

Within the last few years a method [1] of estimating the prothrombin content of plasma has been described and is now being used successfully in a number of clinics. To the plasma of oxalated blood is added a measured excess of a tissue thromboplastin (rabbit brain) and then an optimal amount of calcium. The interaction of the prothrombin content of the specimen with the added reagents yields thrombin which then alters the fibrinogen of the plasma to fibrin,—the plasma coagulates. In this reaction the calcium and the thromboplastin are known values and if it be assumed that the fibrinogen content is normal, then the only unknown is the prothrombin. Hence, any variation in the speed of the reaction may be laid to quantitative or qualitative deficiencies in the prothrombin content of the plasma. When the technic recently described by Quick,[2] is employed normal plasmas will clot in from 12 to 13 seconds after the addition of the calcium. It has been found that when clotting does not occur until 25 to 30 seconds have elapsed, clinical evidence of a bleeding tendency are apt to be seen. Such a lengthening of the clotting time is thought to correspond to a reduction of the prothrombin to 20 to 15 per cent of the normal amount in the plasma. The clotting time in plasma studied by the above technic is spoken of as the "prothrombin time."

A study of hemorrhagic diseases as to their "prothrombin time" has shown that in a few conditions in both animals and man a lengthening of the "prothrombin time" is present in apparently significant association with the bleeding tendency. Such conditions include the hemorrhagic disease of chicks produced by a dietary deficiency; the so-called sweet clover disease of cattle which appears when spoiled sweet clover hay is eaten; instances of severe hepatic injury such as chloroform poisoning; cases of obstruction of the biliary passages with jaundice; and experimental or clinical examples of biliary fistulae. In all of these the tendency to bleed is associated with a lengthening of the "prothrombin time."

An important addition to our knowledge of these types of coagulation defect due to prothrombin deficiency was made by Dam [3] who studied the food constituent whose lack leads to a hemorrhagic disease in chicks, and named it vitamin K or the "koagulation vitamin." Vitamin K is a fat-soluble substance found in cabbage, spinach, alfalfa, hog liver oil and fish meal. It may apparently be formed from some food-stuffs by the action of putrefactive bacteria. It is fairly heat stable. In its more concentrated preparations a dose of 2 to 10 mg. per kilogram of food will protect chicks against the development of the hemorrhagic condition. Likewise, its administration will promptly cure the condition. Tests for the presence of vitamin K in organic material are based upon its protective or curative powers for chick hemorrhagic disease. Since the cure of the disease by vitamin K is

[1] Quick, A. J., Stanley-Brown, M., and Bancroft, F. W.: A study of the coagulation defect in hemophilia and in jaundice, Am. J. Med. Sci., 1935, clxxxx, 501–511.

[2] Quick, A. J.: The nature of the bleeding in jaundice, Jr. Am. Med. Assoc., 1938, cx, 1658–1662.

[3] Dam, H., and Glavind, J.: Vitamin K in human pathology, Lancet, 1938, ccxxxiv, 720–721.

accompanied by a shortening of the "prothrombin time," signifying presumably an increase in plasma prothrombin, this work of Dam's suggests that vitamin K is a necessary ingredient in the synthesis of prothrombin. The fact that in the hemorrhagic sweet clover disease of cattle the increased prothrombin time can be reduced to normal by feeding alfalfa meal which is rich in vitamin K likewise points in the same direction.

Of especial importance in clinical medicine is the application of the knowledge gained by Dam's work and that of others in this field to the problem of bleeding in diseases of the liver and of the bile excretory ducts. In cases of severe injury to liver parenchyma and in cases of obstruction to the bile passages, high grades of jaundice are observed and in the past the retention of bile pigments and of bile salts has been assumed to cause the defect in coagulation which led to bleeding. However, there is only rough parallelism between the degree of jaundice and the danger of bleeding. Moreover, in bile fistula cases the bleeding tendency develops in a severe form in the absence of any jaundice. Jaundice and cholemia per se may therefore be ruled out as the cause of the bleeding tendency in these three conditions. In severe hepatitis and in obstructive jaundice, high grade impairment of some liver functions is present and it might be assumed that in these conditions the injured liver is unable to produce sufficient prothrombin. There is, however, no certainty as to the part played by the liver in the production of prothrombin and, moreover, in experimental bile fistula animals, in spite of the absence of serious liver damage, the "prothrombin time" is lengthened and bleeding occurs.

It is significant that in all three of these conditions bile either does not reach the intestinal tract or reaches it in very much diminished amounts.

Both Judd and Wangensteen some years ago noted this point and advocated the feeding of bile to such patients to lessen the risk of post-operative hemorrhage. This therapy in some instances was of undoubted benefit. Hawkins and Brinkhous[4] in bile-fistula dogs showed that bile feeding brought the prolonged "prothrombin time" back to normal and prevented hemorrhagic phenomena. Both Quick,[5] and Greaves and Schmidt,[6] in 1937, pointed out that the rôle of the bile was probably to aid in the absorption of vitamin K from the diet. Greaves and Schmidt produced a lengthened prothrombin time in rats by biliary fistulae and by ligation of the common duct; they reduced this prothrombin time by giving massive doses of vitamin K or by feeding bile with the diet. Quite recently H. R. Butt, A. M. Snell and A. E. Osterberg[7] have reported a patient with obstructive jaundice and a greatly lengthened prothrombin time in whom the adminis-

[4] Hawkins, W. B., and Brinkhous, K. M.: Prothrombin deficiency the cause of bleeding in bile fistula dogs, J. Exper. Med., 1936, lxiii, 795–801.

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tration daily of large doses of a potent vitamin K preparation orally over a period of one week had no effect in reducing the prothrombin time. The patient was taking no food by mouth. Upon the addition of bile by mouth to the vitamin K preparation, the prothrombin time fell abruptly to almost normal levels. It seems, therefore, highly probable that the presence of bile in the bowel is essential to the absorption of vitamin K. Dam has reported results indicating that if vitamin K be given intramuscularly it will reduce to normal the lengthened prothrombin time in human cases of obstructive jaundice. This method of administration would greatly simplify the therapeutic problem.

Active work is in progress in a number of clinics in the attempt to apply in human therapy the knowledge here briefly outlined. Such information as to results which is available suggests that a valuable aid in the prevention of bleeding in cases of diseases of the liver and bile ducts has been acquired.

REVIEWS

Psychotherapy. By PAUL SCHILDER, M.D., Clinical Director, Psychiatric Division, Belleview Hospital, and Research Professor of Psychiatry, New York University Medical College. 344 pages. W. W. Norton & Co., New York. 1938. Price, $3.50.

The author states that he wrote this book " from a conviction that psychotherapy is not an art but a technical procedure based upon scientific principles." In eleven chapters he develops his hypothesis: (1) Some general principles; (2) Psychophysiological relations; (3) The symptomatology of organic disease from the point of view of psychology; (4) The symptomatology of mental suffering; (5) Symptoms which make others suffer; (6) Somatic health as an experience; (7) Psychic health as an experience; (8) Technical tools of psychotherapy; (9) The relation between physician and patient; (10) The psychotherapeutic systems; (11) The treatment of specific types of neuroses, psychopathies, and psychoses. Dr. Schilder further states that this book is intended for students, physicians and psychiatrists, although he expects others to read it. Nevertheless, he emphasizes that " Psychotherapy is the task of the physician."

The author has a wide experience, and he fairly presents the various systems of psychotherapy, perhaps taking up most of his discussion with the subject of psychoanalysis. He feels that many physicians use psychoanalytic principles, but refuse to admit this fact, and that they should not hide it. Case histories are not given because he feels that they are never studied.

Dr. Schilder has presented very little new, but there is no doubt a need for a book of this kind, and it can be recommended to the internist.

J. L. McC.

The Diagnosis and Treatment of Diseases of the Liver and Biliary Tract. By JOHN PHILLIPS, M. B., late chief of Medical Division, The Cleveland Clinic, Cleveland, Ohio; Revised by RUSSELL L. HADEN, M.D., Head of Department of Medicine, The Cleveland Clinic. HENRY A. CHRISTIAN, M.D., Sc.D., LL.D., General Editor of the Series. Oxford University Press, New York. 1936.

This volume is one of the Oxford Monographs on Diagnosis and Treatment. Having for a long time been interested in diseases of the liver, Dr. Phillips had just completed the manuscript for the book at the time of his death as a result of the Cleveland Clinic fire.

The subject matter is well presented, the print is large and easily read and there are a number of excellent illustrations. A bibliography is furnished at the end of each chapter. The fact that there are comparatively few references after 1930 is doubtless due to the circumstances noted above.

The volume may be recommended to students and to practitioners as a sufficiently complete discussion of the diagnosis and treatment of the diseases concerned.

T. P. S.

Practical Bacteriology, Haematology, Parasitology. By E. R. STITT, M.D., Sc.D., LL.D., PAUL W. CLOUGH, M.D. and MILDRED C. CLOUGH, M.D. 961 pages; 14.5 × 21.5 cm. Ninth Edition. B. Blakiston's Son and Co., Inc., Philadelphia. 1938. Price, $7.00.

The new edition of this long accepted standard reference work still maintains the high place among similar works that has been held by former editions. The

revising authors have made many extensive changes in arrangement of subject material, condensations of topics, and have added 113 pages to the text. The original principle of a text for those with limited library facilities has been adhered to. However, the book contains many things not to be found in similar works. The chapter on fungi is particularly helpful. The section on hematology has been much enlarged and two color plates added. The chapter on "Serological Methods" might have included the Kline test for syphilis to advantage. The title, though long, does not indicate the scope covered by the text. A subtitle "Complete Diagnostic Guide" might be more accurate. Any physician may profit from the final section entitled "Laboratory Procedures Useful in Diagnosis, Indexed by Diseases."

J. H. M.

The Thyroid and Its Diseases. By J. H. MEANS, M.D. 602 pages; 23 × 15.5 cm. J. B. Lippincott Co., Philadelphia. 1937. Price, $6.00.

Many physicians especially interested in the diseases of the thyroid have already studied this excellent monograph, but it is deserving of notice by a larger group of internists. Its peculiar value lies in the fact that it is the presentation of the well matured experience of an active thyroid clinic, that of the Massachusetts General Hospital, rather than a survey of the world literature. It presents in detail the point of view attained from personal experience as well as the carefully collected data upon which this point of view is based. There is no attempt to cover the entire field with equal thoroughness; no important topics are omitted, but those which have been the subject of especial investigation in the Clinic are dealt with at greater length. The chapters on myxedema and on the iodine response in toxic goiter summarize the important contributions of the author to these subjects.

There are seven chapters dealing with such subjects as the anatomy of the thyroid, the thyroid hormone, the relation of the thyroid to other endocrine glands, thyroid pathology and symptomatology, methods of examination and classification. Chapters VIII to XX deal with the diseases of the thyroid; simple goiter, myxedema, cretinism, toxic goiter and associated topics, nodular goiter, thyroiditis and anomalies of the thyroid. There are two further chapters, one on the topic of thyroid administration in diseases of other than thyroid origin, and one on total thyroidectomy in diseases of other than thyroid origin. The final chapter contains a critical consideration of what is known of the significance of thyroid function, of thyreotoxicosis, of hypothyroidism and of the nature of the iodine response. At the end of each chapter there is a brief summary and a bibliography.

The author has positive opinions and states them plainly. At the same time he is not dogmatic and readily confesses to the lack of answer at present to many of our important queries. In classification he groups all toxic cases together considering that there is little practical value in distinguishing, as is done at the Mayo Clinic, between exophthalmic goiter and adenomatous goiter with hyperthyroidism. He has found that as little as six milligrams of iodine a day will give a full iodine response but sees the advantage in routinely using a much larger dose. The etiology of the thyroid crisis is still to him obscure. He discusses in an interesting way the diagnostic value of the iodine remission, the value of vitamin B therapy and innumerable other special topics.

Dr. Means' volume is an important addition to the literature of thyroid disease, and a manual of great practical value to the internist and surgeon.

M. C. P.

COLLEGE NEWS NOTES

New Life Member

Dr. Arthur T. Newcomb, F.A.C.P., Pasadena, Calif., became a Life Member of the American College of Physicians on May 31, 1938, through regular subscription to the Endowment Fund.

Gifts to the College Library

Grateful acknowledgment is made of the receipt of the following donations to the College Library of publications by members:

Reprints

Lt. Col. C. L. Beaven, F.A.C.P., (MC), U. S. Army, 3 reprints: "The Doctor Stays at Home";

Dr. Richard E. Ching, F.A.C.P., Memphis, Tenn., 4 reprints: "Hypertensive Disease: Basic Factors and Management": "Pathology of Sicle Cell Anemia" "Splenectomy in Sicle Cell Anemia"; "Recent Advances in the Treatment of Pneumonia";

Dr. Anthony C. Cipollaro (Associate), New York, N. Y., 1 reprint: "Treatment of Cutaneous Tuberculosis";

Dr. Barnett Greenhouse (Associate), New Haven, Conn., various manuscripts and publications dealing with nutrition, diabetes and obesity;

Dr. Louis L. Perkel (Associate), Jersey City, N. J., 3 reprints: "The Role of Roentgen Diagnosis in Gastrointestinal Diseases"; "Gastric Polyposis"; "Toxic Hepatitis (Acute Yellow Atrophy) Due to Cinchophen (Atophan)";

Dr. Eugene S. Sugg (Associate), New York, N. Y., 2 reprints: "Acquired Sensitivity to Cinchophen";

Capt. Ralph M. Thompson (Associate), (MC), U. S. Army, 2 reprints: "Lymphopathia Venereum"; "Gonococcic Endocarditis."

Dr. Peter Irving, F.A.C.P., Executive Secretary of the Medical Society of the State of New York, has contributed the 1938 Medical Directory of New York, New Jersey and Connecticut, a valuable index and directory to all physicians in those States.

Mr. Louis Brownlow, Editor, has donated a copy of the new edition, 1938–39, of "Public Administration Organizations—A Directory" to the Library of the College. This Directory lists and describes the voluntary, unofficial associations, organizations and agencies which have some direct or apparent relationship to the processes of public administration. The national organizations are classified by fields of activity, such as education, forestry hospital administration, housing, insurance, justice, labor, library administration, public welfare, public works, recreation, safety, taxation, universities and colleges, etc., etc.

Sectional Meeting of Montana Members

On May 14, 1938, Fellows and Associates of the American College of Physicians resident in Montana held a meeting at the Montana Club in Helena, under the leader-

ship of Dr. Louis H. Fligman, F.A.C.P., Governor of the College for Montana. Every member, both Fellow and Associate, in the State of Montana was present, with the exception of one, who unavoidably had to be in Chicago—a remarkable showing when distance and difficulties of transportation in that large State are considered.

It was felt that in order to identify these members more closely with the College, the name formerly used, Montana Society of Internists, should be dropped and henceforth the group will be known as the Montana Branch of the American College of Physicians. Dr. Fligman was reëlected President of the group for the ensuing year; Dr. W. G. Richards, F.A.C.P., of Billings, Vice-President; Dr. H. C. Watts, F.A.C.P., of Fort Harrison, Secretary.

Dr. A. R. Foss, F.A.C.P., of Missoula presented an intensely interesting and thoughtful paper on the subject of diabetes. Each one of the physicians present took part in the discussion. It is felt that this local organization will be productive of great good, not only to the individual physicians concerned, but to the cause of scientific internal medicine in that State.

Dr. George W. McCoy, F.A.C.P., for many years attached to the U. S. Public Health Service at Washington, D. C., has accepted the appointment as head of the department of preventive medicine at Louisiana State University School of Medicine, New Orleans, beginning September, 1938. Dr. McCoy will retain his status as an active member of the U. S. Public Health Service and will carry on his epidemiologic studies of leprosy.

Dr. McCoy was a native of Cumberland Valley, Pa., and was graduated from the University of Pennsylvania School of Medicine in 1898. He was first appointed assistant surgeon of the Public Health and Marine Hospital Service in 1905, and surgeon in the U. S. Public Health Service in 1913. He was named medical director of the Service in 1930. He was in charge of the U. S. Plague Laboratory, San Francisco, from 1908 to 1911, and was director of the U. S. Leprosy Station from 1911 to 1915, serving also during this period as sanitary adviser to the government of Hawaii. He served as director of the National Institute of Health, formerly known as the Hygienic Institute, from 1915 to 1937, and he was president of the Washington Academy of Sciences in 1935. He has been an examiner and member of the Basic Science Board and the National Board of Medical Examiners, a member of the Council on Pharmacy and Chemistry of the American Medical Association and a member of the U. S. Pharmacopoeia Revision Committee.

At the recent annual meeting of the American Gastro-Enterological Association during May, it was decided to hold the next meeting of this body May 1 to 2, 1939, at the Hotel Claridge, Atlantic City. The following officers were elected for the coming year: Dr. Ernest H. Gaither, F.A.C.P., Baltimore, President; Dr. Irvin Abell, F.A.C.S., Louisville, First Vice President; Dr. Andrew C. Ivy, F.A.C.P., Chicago, Second Vice President; Dr. Russell S. Boles, F.A.C.P., Philadelphia, Secretary; Dr. A. H. Aaron, F.A.C.P., Buffalo, Treasurer; Dr. Sara M. Jordan, F.A.C.P., Boston, Recorder; Dr. Howard F. Shattuck, F.A.C.P., New York, Dr. Chester M. Jones, F.A.C.P., Boston, and Dr. Ralph C. Brown, Chicago, Members of the Council.

Dr. J. C. Geiger, F.A.C.P., Director of Public Health for the City and County of San Francisco, was the recipient of the honorary degree of Doctor of Laws at the

commencement of the University of Santa Clara on June 4, in recognition of his humanitarian activities in the public service.

Dr. E. J. G. Beardsley, F.A.C.P., Philadelphia, gave a clinic at the Pottsville (Pa.) Hospital, April 28, 1938, as part of the Schuylkill County Medical Society's Postgraduate Seminar.

Dr. C. H. Cocke, F.A.C.P., Dr. Paul Ringer, F.A.C.P., Dr. M. L. Stevens, F.A.C.P., and Dr. Karl Schäffle, F.A.C.P., the latter as chairman, are members of a committee that conducted a seminar in tuberculosis at Asheville, N. C., during July, 1937, and are preparing to repeat the seminar this year, July 11 to 16.

Dr. Samuel M. Feinberg, F.A.C.P., Chicago, addressed the Regional Allergy Society (Indiana, Kentucky, and Southern Ohio) at Cincinnati on May 22, his subject being "The Rôle of Air-Borne Fungi in Allergy."

Dr. Samuel E. Munson, F.A.C.P., Governor of the College for Southern Illinois, Springfield, was inducted as President of the Illinois State Medical Society at its meeting in Springfield during May. Dr. James H. Hutton, F.A.C.P., Chicago, was chosen President-Elect. Dr. Cecil Jack, F.A.C.P., Decatur, is Chairman of the Medical Section.

Dr. Robinson Bosworth, F.A.C.P., East St. Louis, Ill., President of the Illinois Tuberculosis Association, has received a joint invitation from the Michigan State Medical Society and the Michigan Tuberculosis Association to give a series of five lectures on tuberculosis to medical societies in five Michigan cities during the month of September.

For several years a series of lectures on diseases of children has been given under the auspices of the Pediatric Department of the University of Louisville School of Medicine under the chairmanship of Dr. Philip F. Barbour, F.A.C.P. A similar series has been under way since April 27, given on Wednesday of each week for ten weeks at the Children's Free Hospital, Louisville.

Dr. Malcolm T. MacEachern, F.A.C.P., Chicago, addressed the fifteenth annual convention of the Minnesota Hospital Association at Minneapolis, May 19 to 21, on "Organization for the Care of the Sick."

Dr. Bernard Fantus, F.A.C.P., Chicago, and Dr. Albert M. Snell, F.A.C.P., Rochester, Minn., addressed the fifty-first annual convention of the North Dakota State Medical Association at Bismarck, N. D., May 16 to 18, on "Some Useful Prescriptions" and "Diagnosis and Treatment of Cholecystic Disease; Recent Studies on Obstructive Jaundice," respectively.

Dr. B. B. Vincent Lyon, F.A.C.P., Philadelphia, and Dr. Frank J. Heck, F.A.C.P., Rochester, Minn., addressed the fifth annual graduate assembly of the Har-

risburg (Pa.) Academy of Medicine, May 4, on "Diagnosis and Management of Peptic Ulcer" and "Treatment of the Anemias," respectively.

Dr. Sigmund S. Greenbaum, F.A.C.P., Dr. Baldwin L. Keyes, F.A.C.P., Dr. Louis B. Laplace, F.A.C.P., and Dr. George Harlan Wells, F.A.C.P., all of Philadelphia, are members of a board of physicians appointed to advise the newly organized Philadelphia Diabetic Society. This Society has been formed by a group of Philadelphia women and a four point program has been adopted. It proposes to make insulin available within the means of all who need it; it will assist diabetics in good condition to find employment; it will have a program of education, both for victims of the disease and for the public, in regard to recognizing early symptoms and the importance of early medical care; the Society will further help unfortunate persons to raise funds for appliances, crutches and artificial limbs, and will help provide camps for children afflicted with diabetes.

Under the Presidency of Dr. Charles H. Turkington, F.A.C.P., Litchfield, the Connecticut State Medical Society held its one hundred and forty-sixth annual meeting at Groton, June 1 to 2. Dr. Theodore G. Klumpp (Associate), Washington, D. C., Chief Medical Officer of the Food and Drug Administration, and Dr. Francis M. Rackemann, F.A.C.P., Boston, addressed the convention on "Drug Problems" and "Skin Tests to Foods and Dusts," respectively.

Dr. David Riesman, F.A.C.P., Philadelphia, delivered the Shattuck Lecture on "America's Contribution to Nosography" before the one hundred and fifty-seventh annual meeting of the Massachusetts Medical Society at Boston, May 31 to June 2.

Dr. Hillyer Rudisill, Jr., F.A.C.P., Charleston, is a member of a commission recently organized to gather, preserve and publish when possible material on the history of the South Carolina Medical Association.

Dr. Seale Harris, Sr., F.A.C.P., Birmingham, was elected President of the Medical Association of the State of Alabama at its last annual meeting in April, succeeding Dr. Edward S. Sledge, F.A.C.P., Mobile.

Dr. Homer Davis, F.A.C.P., Genoa, was inducted as President of the Nebraska State Medical Association at its last annual session in Lincoln, April 28.

The American Heart Association held its fourteenth scientific session in San Francisco, June 10 to 11, under the presidency of Dr. William J. Kerr, F.A.C.P. and President of this College. Dr. Kerr's presidential address was on "Relief of Pain in Angina Pectoris Through Improved Filling of the Heart." Dr. Carl J. Wiggers, F.A.C.P., Cleveland, delivered the annual address on "The Dynamics of Hypertension."

Examinations by American Board of Pediatrics

The American Board of Pediatrics has announced the following dates for future examinations:

Detroit, October 26 (Wednesday), preceding the meeting of Region III of the American Academy of Pediatrics;
Rochester, N. Y., November 13 (Sunday), following the meeting of Region I of the American Academy of Pediatrics;
Oklahoma City, November 15 (Tuesday), preceding the joint meeting of Region II of the Academy with the Southern Medical Association.

The Board announces that all applications must be in the office of the Secretary, Dr. Charles A. Aldrich, Winnetka, Ill., at least four months in advance of an examination. The Board has ruled that applicants who have failed at one examination must wait two years before coming up for reëxamination, and must show evidence of further study or training to justify reëxamination.

Dr. William A. Groat, F.A.C.P., Syracuse, N. Y., was inducted as President of the Medical Society of the State of New York at its annual session in New York City May 9 to 12, 1938.

OBITUARIES

DR. SANFORD MARTIN WITHERS

Dr. Sanford Withers, aged 46 years, died March 8, 1938, at the Rockefeller Institute for Medical Research, New York City of aplastic anemia induced by over-exposure to the action of radium.

Dr. Withers was born on November 25, 1891, in Clearwater, Missouri. After his preliminary education he entered Washington University Medical School in St. Louis but before graduation his study was interrupted by a year's service in France with Base Hospital No. 21. After discharge from the Army, he reëntered medical school and was graduated in 1919. After his internship in Barnard Skin and Cancer Hospital in St. Louis he did postgraduate work at the Memorial Hospital in New York City. In 1921 he came to Denver and was for one year medical director of the Radium Company of Colorado. After a year with this company he entered private practice which he continued until the time of his death. He was a Fellow of the American College of Physicians since April 4, 1932, a member of the American College of Radiology, the American Board of Radiology and the British Institute of Radiology. He was a member, ex-president and ex-treasurer of the American Radium Society. He was a member of the American Society for the Control of Cancer and was chairman of the Cancer Committee in Colorado for this organization. He belonged to the American Medical Association, the Denver Radiological Club, the Medical Society of the City and County of Denver, the Colorado State Medical Society and served as chairman of the State Committee on Cancer Education. He was a member of Rouen Post No. 21 of the American Legion, the Emulation Lodge No. 154 of Denver, Consistory No. 1 of Denver and the Phi Rho Sigma medical fraternity. At the time of his death he was director of the Radiation Therapy Department of the Denver General Hospital. He was the author of numerous technical articles and books.

In spite of a frail physique and much ill-health during the last ten years of his life, Dr. Withers did a prodigious amount of work of the highest quality. His unceasing efforts to equip himself to do the best work in his chosen field won for him national recognition.

He is survived by his wife and two children.

JAMES J. WARING, M.D., F.A.C.P.
Governor for Colorado.

DR. ROSS VERNET PATTERSON

Dr. Ross Vernet Patterson (Fellow), Philadelphia, Pa., for twenty-two years Dean of the Faculty of the Jefferson Medical College, Philadelphia, died on May 2, 1938. He was fortunate in having to endure only a few weeks of disabling illness that was due to complications of long-existing hypertensive cardiovascular disease.

Ross V. Patterson was born October 5, 1877, in New Orleans, La. He was the son of John Harrison Patterson and Margaret Jane (Orcutt) Patterson. His ancestral antecedents were of Scotch and English descent and they were among the early pioneers of the State of Illinois.

Dr. Patterson's pre-medical education was obtained at the Chenet's Institute, New Orleans, in the public schools of Colorado Springs, Colo., and in the Central College in Missouri. His first two years in medicine were spent at the Washington University, St. Louis, Mo., after which he matriculated at the Jefferson Medical College, from which institution he graduated in 1904. He served his internship at the Philadelphia General Hospital and later he continued in the same institution as Assistant Physician to the Department for the Insane and as Assistant Chief Resident Physician. In the autumn of 1906, Dr. Patterson became the Assistant Executive Officer at the Jefferson Medical College, under Professor James W. Holland, the Dean of the College. At this time, he entered private practice and became associated with the teaching staff of the College as an Instructor in Medicine. In 1908, there was established an electrocardiographic station at the Jefferson Hospital and Dr. Patterson was given charge of the Department. In 1916, Dr. Patterson succeeded Dr. Holland as Dean of the College and from this time devoted the greater portion of his time and thought to its interests.

Dr. Patterson was Visiting Physician to the Jefferson, Episcopal and Philadelphia General Hospitals and served as Consultant to a number of other city hospitals. In 1934, Dr. Patterson succeeded the late Professor Hobart A. Hare as Professor of Therapeutics at the Jefferson Medical College. As a teacher of medicine and therapeutics, Dr. Patterson was systematic, painstaking, conservative and helpful.

Dr. Patterson was prominent in medical and social circles. He was President of the Medical Society of the State of Pennsylvania in 1930, and served as President of the Association of American Medical Colleges for two terms. Dr. Patterson was a Fellow of the Philadelphia College of Physicians, and a Fellow of the American College of Physicians since 1923. He was a veteran member of the American Therapeutic Society, and an active member of the American Heart Association.

When the World War came, Dr. Patterson wished to enter the military service, but the Surgeon General ordered him to remain at his post as Dean of the Medical College. Although Dr. Patterson did not enter active military service, he accomplished far more for the Medical Corps than if he had been in uniform. He was, with Dr. W. M. L. Coplin, largely responsible for securing funds and equipment for the Jefferson Medical College Hospital's Base Hospital unit. For a number of years, Dr. Patterson has been a Lieutenant Colonel in the Medical Reserve Corps, U. S. Army.

In 1928, the Governor of Pennsylvania appointed Dr. Patterson a member of the Commission to study the laws relating to the healing art and, in connection with this important task, his sound judgment and general

helpfulness commanded the admiration of all with whom he came in contact. Dr. Patterson is said to be the author of the law creating the State Board of the Healing Art, introduced in the Pennsylvania Legislature in 1931.

The honorary degree of Doctor of Science was conferred upon Dr. Patterson by LaSalle College in 1931, and the same degree was awarded by Colgate University in 1932. Ursinus College awarded Dr. Patterson the honorary degree, LL.D., in 1935, and Wake Forest College, in 1937.

Dr. Patterson was an active member of the Phi Alpha Sigma National Medical Fraternity and served this organization as its Primarius Magnus in 1907. He served as President of the Alumni Association of the Jefferson Medical College for three terms. He was a member of the Union League of Philadelphia and of the Art and University Clubs. Dr. Patterson was an enthusiastic sportsman and was deservedly popular in sport circles. Later in life than is the rule, Dr. Patterson became enthusiastically interested in trap shooting, and was an active member of the Quaker City and Roxborough Gun Clubs. He was serving the latter organization as its Vice President at the time of his death.

Ross V. Patterson was a positive character, and he possessed a host of firm friends and admirers. He will be missed by his friends and it will be difficult to replace him as an extremely efficient and talented executive officer of an independent medical college.

E. J. G. Beardsley, M.D., F.A.C.P.,
Philadelphia, Pa.

ABSTRACTED AND CONSOLIDATED MINUTES OF THE BOARD OF REGENTS

Meeting No. 1

The first meeting of the Board of Regents of the American College of Physicians, during the New York Session, convened April 3, 1938, at the Waldorf-Astoria Hotel, New York City, with President James H. Means presiding, with Mr. E. R. Loveland acting as secretary and with an attendance of twenty-two members of the Board present.

Under communications, Dr. James E. Paullin, Chairman of the Committee on Public Relations, presented letters of resignations from three Fellows and four Associates; two resignations were from pediatricians who expressed their primary interest in pediatric societies. Dr. Paullin, in presenting these resignations, pointed out that they should be received with regret, because pediatricians should be retained in the College not only from the standpoint of the benefit accruing to them, but from the standpoint of the benefit other College members receive. For the Committee on Public Relations, Dr. Paullin presented the suggestion that the Board of Regents consider the possibility of reducing the annual dues of specialists, other than internists, since such specialists must also maintain their memberships in their own special societies. The reduction of such dues, he felt, would stimulate their continued interest in the College, and it would redound to the benefit of the College. The resignations from Associates were in some instances occasioned either by lack of interest in the work of the College or by anticipation of inability to qualify for Fellowship.

On motion by Dr. O. H. Perry Pepper, seconded by Dr. Walter W. Palmer, and regularly carried, it was

Resolved, that the resignations of the following be accepted:

Dr. Amos C. Gipson (Fellow), Gadsden, Ala.
Dr. Joseph M. Ulrich (Fellow), Akron, Ohio
Dr. Henry C. Wales (Fellow), Toronto, Ont.
Dr. Raymond Maine Rice (Associate), Indianapolis, Ind.
Dr. Arthur G. Schoch (Associate), Dallas, Tex.
Dr. Floyd W. Stevens (Associate), Scranton, Pa.
Dr. J. Wm. Wood (Associate), Chester, Pa.

A general discussion followed concerning the advisability of lowering the annual dues of the College to $10.00 for all specialists, other than internists. It was pointed out, however, that this would be equivalent to penalizing the regular members of the College by making them pay higher dues, because they are internists, than other members, because they are specialists in other fields, would have to pay. It was pointed out that the College has gone on record with regard to the admission of physicians engaged in the specialties allied to Internal Medicine, and that it was unanimously voted to retain such specialists in the College and to encourage other qualified physicians in these specialties to join.

Dr. William J. Kerr suggested the possibility that the College could furnish men in the allied specialties with one of the special journals in their specialty as a part of their membership in the College, instead of reducing the dues for them.

Dr. Jonathan C. Meakins denounced the whole idea of having graded Fellowships, and Dr. Ernest B. Bradley expressed the belief that a reduction of $5.00 would not be of material help. Dr. O. H. Perry Pepper and Dr. James Alex. Miller both

expressed their opposition to the problem, and a motion by Dr. James B. Herrick and Dr. William D. Stroud, suggesting a postponement of action, was withdrawn.

On the recommendation of the Committee on Public Relations, certain specific cases affecting fees and dues were disposed of by special and individual action. After the reading of a communication from the City of Minneapolis, Division of Hospitals, asking for a ruling by the College regarding the age limit for patients admitted to the pediatric service, the Board ruled that inasmuch as this is purely an administrative problem, it should be determined entirely by local conditions and no ruling should be recommended by the College. After the reading of a communication from the Niemann and Northcutt Clinic, of Ponca City, Okla., asking the College to pass upon certain fees scheduled by various organizations for the Ponca City Hospital, the Board ruled that this question should be handled by local authorities and the local county medical society, in coöperation with the American Medical Association.

After the presentation of a communication complaining that the American College of Chest Physicians had simulated very greatly the title of the American College of Physicians and had adopted as a part of its Seal the identical cut of "Laennec" as used by the College on its John Phillips Medal, the Board adopted a resolution protesting the use of the name of the American College of Chest Physicians and requesting that organization to change its name on the grounds that the present name is an infringement upon the priority rights of the American College of Physicians.

A communication was read from the California Society for the Promotion of Medical Research, dealing with a bill recently introduced into the California Legislature, to be voted on in 1938, known as the "State Humane Pound Law," which will tremendously cripple animal experimentation and impair medical research not only in California, but in other parts of the country, if passed. After general discussion, the Board adopted a resolution providing that a committee be appointed to draw up a suitable resolution before the next Regents' meeting.

Two communications were presented complaining about the activities of two different Fellows of the College, whereupon, at the recommendation of the Committee on Public Relations, the Board adopted a resolution that no action could be taken unless specific charges are directly preferred in accordance with the Constitution and By-Laws of the College.

The Secretary-General, Dr. George Morris Piersol, reported the following deaths since the last meeting of the Board of Regents:

Fellows:

Brown, Lawrason	Saranac Lake, N. Y.	December 26, 1937
Burns, Michael A.	Philadelphia, Pa.	March 7, 1938
Cherry, Solomon L.	Clarksburg, W. Va.	October 21, 1937
Davis, Stephen Webb	Charlotte, N. C.	March 16, 1938
Eastmond, Charles	Brooklyn, N. Y.	November 27, 1937
Futcher, Thomas B.	Baltimore, Md.	February 25, 1938
Houghton, E. Mark	Detroit, Mich.	December 12, 1937
Moore, C. Ulysses	Portland, Ore.	December 21, 1937
Orbison, Thomas James	Los Angeles, Calif.	March 26, 1938
Smith, Thomas Cook	Louisville, Ky.	December 14, 1937
Tarkington, Grayson E.	Albuquerque, N. M.	January 12, 1938
Wellman, Harvey E.	Providence, R. I.	October 20, 1937

Associates:

Grayson, Cary T.	Washington, D. C.	February 15, 1938
Jaeger, Henry W.	Washington, D. C.	October 21, 1937
Lee, John	Detroit, Mich.	September 22, 1937
Montgomery, John L.	Los Angeles, Calif.	January 24, 1938
Patterson, Harrie A.	Fort Stanton, N. M.	October 30, 1937
Ver Nooy, Charles D.	Cortland, N. Y.	January 20, 1938

Dr. Piersol presented the following list of new Life Members since the last meeting of the Board of Regents:

Louis H. Fligman	Helena, Mont.
Max. H. Weinberg	Pittsburgh, Pa.
Walter P. Anderton	New York, N. Y.
Orrin Sage Wightman	New York, N. Y.
J. Corwin Mabey	Montclair, N. J.
Robert L. Levy	New York, N. Y.
Harry S. Emery	Portland, Maine
Alex. M. Burgess	Providence, R. I.
Theodore S. Bacon	Springfield, Mass.
Mary Riggs Noble	Bowmansdale, Pa.
Mary Elizabeth Bass	New Orleans, La.
Karl Vogel	New York, N. Y.
Charles Ricksher	Norwich, Conn.
Floyd Heaton Lashmet	Petoskey, Mich.
John Paul Ritchey	Missoula, Mont.
James F. Churchill	San Diego, Calif.
Emanuel Klaus	Cleveland, Ohio
Harry W. Coffin	Los Angeles, Calif.

Dr. Sydney R. Miller, as Chairman of the Committee on Credentials, reported that the Committee on Credentials had held a meeting at the College Headquarters in Philadelphia on March 6 and another meeting at New York City on April 3, and, after reviewing the credentials of candidates for Fellowship and Associateship, Dr. Miller's analysis of the recommendations of the Committee on Credentials was as follows:

Associates	*March 6*	*April 3*	*Total*
Recommended for Election	79	50	129
Deferred for further credentials	3	4	7
Found not qualified	12	2	14
Withdrawn	1		1
			151

Fellows	*March 6*	*April 3*	*Total*
Recommended for Election:			
Advanced from Associateship	79	25	104
Direct elections to Fellowship	8	5	13
Recommended for election to Associateship first	1	1	2
Deferred for further credentials	6	8	14
Found not qualified		1	1
			134

On motion by Dr. Sydney R. Miller, seconded by Dr. Charles H. Cocke, and regularly carried, it was

RESOLVED, that the following physicians be and are herewith elected to Fellowship or Associateship as designated.

For Fellowship:

Name	*City and State*
1. Anderson, Otis Leon	Richmond, Va.
2. Arrington, George Lamar	Meridian, Miss.
3. Ashford, Mahlon	New York, N. Y.
4. Bach, Theodore Franklin	Philadelphia, Pa.
5. Baird, John Adams	Dayton, Ohio
6. Baldwin, Francis William	New York, N. Y.
7. Barrett, Raymond Lathrop	Springfield, Mass.
8. Bauer, Louis Hopewell	Hempstead, N. Y.
9. Bennett, Clarence Rhodes	Eufaula, Ala.
10. Bixby, Edward Welles	Wilkes-Barre, Pa.
11. Bizzozero, Orpheus Joseph	Waterbury, Conn.
12. Black, Everett O.	Johnson City, N. Y.
13. Brennan, Joseph Patrick	Pendleton, Ore.
14. Brewer, Timothy F.	Hartford, Conn.
15. Brines, Osborne Allen	Detroit, Mich.
16. Burns, Gerald Ross	Halifax, N. S., Can.
17. Canelo, Clarence Kelly	San Jose, Calif.
18. Carruthers, Lyman Bruce	New York, N. Y.
19. Collins, Leon Howard, Jr.	Philadelphia, Pa.
20. Collmann, Xavier Kuehn	Wilkes-Barre, Pa.
21. Connelly, Richard Campbell	Detroit, Mich.
22. Conwell, Daniel Vincent	Halstead, Kan.
23. Corrigan, George Francis	Wichita, Kan.
24. Dardinski, Vincent Joseph	Washington, D. C.
25. Decherd, George Michael, Jr.	New Orleans, La.
26. Durant, Thomas Morton	Philadelphia, Pa.
27. Eastland, John Sheldon	Baltimore, Md.
28. Edson, Philips Josiah	Pasadena, Calif.
29. Fetter, Ferdinand	Philadelphia, Pa.
30. Finch, Russell Leslie	Lansing, Mich.
31. Finucane, Daniel Leo	Glenn Dale, Md.
32. Fisher, Luther Irvin	Bethlehem, Pa.
33. Flowers, Hiland L.	New York, N. Y.
34. Fox, Everett Clarence	Dallas, Tex.
35. Freston, Julian Maxwell	New York, N. Y.
36. Gardiner, John Francis	Omaha, Nebr.
37. Gillick, David Walter	Shawnee, Okla.
38. Gordon, Abraham S.	Brooklyn, N. Y.
39. Gordon, Harold	Louisville, Ky.
40. Graczyk, Stephen A.	Buffalo, N. Y.
41. Grayson, William Bandy	Little Rock, Ark.
42. Greenspun, David Stoven	Bridgeport, Conn.
43. Halprin, Harry	Caldwell, N. J.
44. Healy, Michael Gerard	M.C., U. S. Army
45. Hitzrot, Lewis Haler	Mercersburg, Pa.
46. Hoffman, Kelse Monjar	Franklin, Pa.

Name	*City and State*
47. Horan, Thomas Neil	Detroit, Mich.
48. Howe, Harland Fallis	Toledo, Ohio
49. Jarratt, Guy Carleton	Vicksburg, Miss.
50. Johnson, George Stephen	San Francisco, Calif.
51. Keltz, Bert Fletcher	Oklahoma City, Okla.
52. Kennedy, Allan Souter	Hamilton, Ont., Can.
53. Kennedy, Paul Augustin	Englewood, N. J.
54. Keyes, Baldwin Longstreth	Philadelphia, Pa.
55. Knighton, James Edward, Jr.	Shreveport, La.
56. Kramer, David Warren	Philadelphia, Pa.
57. Kullman, Harold John	Detroit, Mich.
58. Lambert, Luther Rush	Fairmont, W. Va.
59. Landry, Arthur Bernard	Hartford, Conn.
60. Levinson, Samuel A.	Chicago, Ill.
61. Mack, Clifford Wilmot	Livermore, Calif.
62. Masters, Thomas Davis	Springfield, Ill.
63. Mathews, William Rosier	Shreveport, La.
64. Maynard, Edwin Post, Jr.	Brooklyn, N. Y.
65. McGee, Lemuel C.	Elkins, W. Va.
66. McKay, Donald R.	Buffalo, N. Y.
67. Miller, James Roscoe	Chicago, Ill.
68. Miller, Merle Middour	Philadelphia, Pa.
69. Millet, Roscoe Frick	Macomb, Ill.
70. Minor, John	Washington, D. C.
71. Misko, George Harold	Lincoln, Nebr.
72. Moench, L. Mary	New York, N. Y.
73. Molitch, Matthew	Atlantic City, N. J.
74. Moore, Norman Slawson	Ithaca, N. Y.
75. Moser, Rollin Henry	Indianapolis, Ind.
76. Myers, Walter Kendall	Washington, D. C.
77. Painter, Jesse Carl	Dubuque, Iowa
78. Pardee, Harold Ensign Bennett	New York, N. Y.
79. Perkin, Frank Scott	Detroit, Mich.
80. Plotz, Milton	Brooklyn, N. Y.
81. Plunkett, John Elmer	Ottawa, Ont., Can.
82. Porter, Ernest Boring	Altadena, Calif.
83. Post, Joseph W.	Philadelphia, Pa.
84. Price, Alvin Edwin	Detroit, Mich.
85. Pruit, Lee Tinkle	Beaumont, Tex.
86. Purdie, Robert McNair	Houston, Tex.
87. Reddick, Walter Grady	Dallas, Tex.
88. Reeves, Rufus Sargent	Philadelphia, Pa.
89. Reichert, Philip	New York, N. Y.
90. Roach, Robert Dickson	Moncton, N. B., Can.
91. Robertson, Harold Frederick	Philadelphia, Pa.
92. Rothenberg, Robert Charles	Cincinnati, Ohio
93. Rubnitz, Abraham S.	Omaha, Nebr.
94. Sanders, Charles B.	Houston, Tex.
95. Schiff, Leon	Cincinnati, Ohio
96. Schultz, Mark P.	Washington, D. C.
97. Scott, Ernest Gerard	Lynchburg, Va.
98. Segar, Laurence F.	Detroit, Mich.
99. Selling, Lowell Sinn	Detroit, Mich.

Name	*City and State*
100. Shapiro, Matthew	New York, N. Y.
101. Smith, Euclid Monroe	Hot Springs National Park, Ark.
102. Smith, Lauren Howe	Philadelphia, Pa.
103. Smith, Percy King	Wichita Falls, Tex.
104. Spain, Will Cook	New York, N. Y.
105. Stalker, Hugh	Grosse Pointe, Mich.
106. Thorp, Edward G.	Boston, Mass.
107. Van Leuven, Buell H.	Petoskey, Mich.
108. Vermilye, Herbert Noble	Forest Hills, N. Y.
109. Walker, William J.	New York, N. Y.
110. Wall, John Cox	Eastman, Ga.
111. Walsh, James C.	Farmingdale, N. Y.
112. Warvel, John Henry	Indianapolis, Ind.
113. Weston, William Graham	Arkansas City, Kan.
114. Wheeler, Daniel Wilbur	Duluth, Minn.
115. White, John Cowles	New Britain, Conn.
116. Wilce, John Woodworth	Columbus, Ohio
117. Wilcox, Clark Anson	Wichita Falls, Tex.
118. Wood, Francis Clark	Philadelphia, Pa.

For Associateship:

Name	*City and State*
1. Abbott, William Osler	Philadelphia, Pa.
2. Andes, Jerome E.	Morgantown, W. Va.
3. Armstrong, Harry G.	M. C., U. S. Army
4. Bach, Luther	Newport, Ky.
5. Bailey, Frederick Randolph	New York, N. Y.
6. Baker, George Erwin	Casper, Wyo.
7. Baker, Wyrth Post	Washington, D. C.
8. Beber, Meyer	Omaha, Nebr.
9. Beck, Frederick	Ithaca, N. Y.
10. Billings, Edward Gregory	Denver, Colo.
11. Bloom, Meyer	Johnstown, Pa.
12. Blotner, Harry	Boston, Mass.
13. Bond, George S.	Indianapolis, Ind.
14. Bower, Albert Gordon	Glendale, Calif.
15. Braceland, Francis James	Philadelphia, Pa.
16. Brosnan, James T.	Worcester, Mass.
17. Brown, Daniel Noyes	New York, N. Y.
18. Bruenn, Howard Gerald	New York, N. Y.
19. Carl, Louie Tate	Memphis, Tenn.
20. Clark, Paul Chester	Syracuse, N. Y.
21. Curb, Dolph Lange	Galveston, Tex.
22. Curtis, John Kimberly	New York, N. Y.
23. Daugherty, John Arthur	Harrisburg, Pa.
24. Davis, Aubrey Milton	Portland, Ore.
25. Davis, Perk Lee	Philadelphia, Pa.
26. Dietrich, Frank Sigel	Rochester, Minn.
27. Douglas, Albert Harris	Jamaica, L. I., N. Y.
28. Dunn, Charles William	Philadelphia, Pa.
29. Elsom, Kendall A.	Philadelphia, Pa.
30. Fallon, Carlos E.	Newburgh, N. Y.

Name	*City and State*
31. Ferguson, Arthur Newton	Fort Wayne, Ind.
32. Flippin, Harrison Fitzgerald	Philadelphia, Pa.
33. Flood, Charles Albert	New York, N. Y.
34. Fry, Franklin Weimer	Hempstead, N. Y.
35. Gardberg, Manuel	New Orleans, La.
36. Gardner, William Alden	New York, N. Y.
37. Garrido Collazo, Jose	Rio Piedras, P. R.
38. Giering, John Fleming	Wilkes-Barre, Pa.
39. Gillespie, James Ogilvie	M. C., U. S. Army
40. Goltz, Harold H.	Clarksburg, W. Va.
41. Green, Mack M.	M. C., U. S. Army
42. Gydesen, Carl Sophus	Colorado Springs, Colo.
43. Hamlin, Harris Howard	Seattle, Wash.
44. Hammond, William	Scarsdale, N. Y.
45. Heffner, Reid Russell	Rochester, Minn.
46. Helmick, John Pierpont	Fairmont, W. Va.
47. Heringhaus, Francis J.	Mansfield, Ohio
48. Herrell, Wallace Edgar	Rochester, Minn.
49. Hess, Charles Leonard	Bay City, Mich.
50. Highberger, Elmer	Oil City, Pa.
51. Hobson, Samuel	New Orleans, La.
52. Holland, Harry Albert	Chestnut Hill, Philadelphia, Pa.
53. Hollingsworth, Merrill Windsor	Santa Ana, Calif.
54. Jaffe, Louis	Detroit, Mich.
55. Jensen, Walter S.	M. C., U. S. Army
56. Jourdonais, Leonard Francis	Evanston, Ill.
57. Juster, Irving R.	Glens Falls, N. Y.
58. Kaufman, Samuel Russel	Wilkes-Barre, Pa.
59. Kelchner, Clyde H.	Allentown, Pa.
60. Kelley, William Henry	Charleston, S. C.
61. Kendall, Ralph Emerson	Hartford, Conn.
62. King, Frederick H.	New York, N. Y.
63. Kitchell, James Roderick	Philadelphia, Pa.
64. Kleiber, Estelle Elizabeth	New Brunswick, N. J.
65. Kooperstein, Samuel I.	Jersey City, N. J.
66. Labensky, Alfred	New London, Conn.
67. Lambert, Samuel W., Jr.	New York, N. Y.
68. La Palm, Leo Frederick	Rochester, N. Y.
69. Leiser, Rudolf	Eloise, Mich.
70. Lewis, Benton Oliver	Galveston, Tex.
71. Lightbody, James J.	Detroit, Mich.
72. Lirot, Stephen Leo Robert	Meriden, Conn.
73. London, McKinley	Cleveland, Ohio
74. Lowance, Mason Ira	Atlanta, Ga.
75. Mandelbaum, Harry	Brooklyn, N. Y.
76. Marty, Frederick Nicholas	Syracuse, N. Y.
77. McCutchan, Guy R.	Council Bluffs, Iowa
78. McDaniel, Walter Shaw	Houston, Tex.
79. McEwen, Ernest George	Evanston, Ill.
80. McGan, Harold P.	Albany, N. Y.
81. Mellen, Hyman Samuel	Detroit, Mich.
82. Merryman, Murlin Paul	Louisville, Ky.
83. Miller, Malcolm W.	Philadelphia, Pa.

Name	*City and State*
84. Muether, Raymond Oliver	St. Louis, Mo.
85. Murphy, Alvin E.	St. George, Staten Island, N. Y.
86. Murphy, John Moylan	Detroit, Mich.
87. Musick, Vern H.	Oklahoma City, Okla.
88. Nealon, Stephen William, Jr.	Washington, D. C.
89. Park, Felix Roman	Bala-Cynwyd, Pa.
90. Parker, Hubert McKibban	Kansas City, Mo.
91. Peck, Franklin Bruce	Indianapolis, Ind.
92. Pepper, Dickinson Sergeant	Melrose Park, Pa.
93. Plummer, Norman	New York, N. Y.
94. Porritt, Ross Joseph	Pontiac, Mich.
95. Powers, William Leonidas	Wichita Falls, Tex.
96. Root, Donald H.	Mendon, Ill.
97. Rosenak, Bernard David	Indianapolis, Ind.
98. Routh, Foster Miller	Columbia, S. C.
99. Russell, Theodore Burg	New York, N. Y.
100. Rutledge, Benjamin Huger	Baltimore, Md.
101. Sabater, Juan	Santurce, P. R.
102. Scott, W. Mastin	Shreveport, La.
103. Shanno, Ralph Leopold	Forty Fort, Pa.
104. Sheckles, Lloyd Webster, Jr.	Galveston, Tex.
105. Sherwood, Kenneth Kyler	Seattle, Wash.
106. Short, Charles Lyman	Boston, Mass.
107. Sigler, Louis H.	Brooklyn, N. Y.
108. Smith, Donald Sanford	Ann Arbor, Mich.
109. Steele, Charles William	Lewiston, Maine
110. Steele, Edson H.	Los Angeles, Calif.
111. Stein, Maurice Isaac	Harrisburg, Pa.
112. Stewart, William Crawford	Charleston, W. Va.
113. Taylor, Samuel Gale, III	Chicago, Ill.
114. Teitelbaum, Myer	Ann Arbor, Mich.
115. Thompson, Ivan	Ogden, Utah
116. Thompson, Ralph Mathew	M. C., U. S. Army
117. Thompson, William P.	New York, N. Y.
118. Turner, Carrol Conway	Memphis, Tenn.
119. Tyson, T. Lloyd	New York, N. Y.
120. Walch, Alphonse Edmund	Minneapolis, Minn.
121. Walker, Helen Gertrude	Buffalo, N. Y.
122. Wall, Emmett Daniel	Philadelphia, Pa.
123. Weidman, William Harold	Norwich, Conn.
124. Weilbaecher, Joseph Oswald, Jr.	New Orleans, La.
125. Weiser, Frank A.	Detroit, Mich.
126. Wetherbee, Winthrop, Jr.	Boston, Mass.
127. Wilkinson, George Richard	Greenville, S. C.
128. Zaur, I. Sidney	Bridgeport, Conn.
129. Ziskind, Joseph	New Orleans, La.

Dr. Miller, in reporting upon that group of Associates elected at the 1933 Annual Session, gave the following analysis:

Qualified for advancement to Fellowship	96
Credentials not presented and subsequently dropped	9
Resigned	6
Total, Candidates elected 1933 Session	111

On recommendation of the Committee on Credentials, the Board of Regents adopted a resolution providing for the discontinuance on the Associateship Roster of seven Associates elected in 1933 who had failed to qualify for Fellowship by presentation of credentials according to the Constitution and By-Laws; also one from the Fellowship Roster who had failed to take up election within the period of one year as provided in the regulations.

Dr. William J. Kerr, Chairman of the Committee on Postgraduate Education, reported as follows:

"Mr. President, Regents, there are two phases of the postgraduate work upon which I shall report separately. The Committee, consisting of Dr. Hugh J. Morgan, Dr. Charles H. Cocke and myself, was increased during the year by the appointment of Dr. Charles Sidney Burwell and Dr. Joseph A. Capps, but neither of these two had been able to be present to participate in our discussion. The first part of our report concerns itself with the postgraduate courses which were given this year for the first time. We had some difficulty and delay in getting under way to determine exactly what type of course should be offered, when it should be given and then the details concerning the type of instruction. It was not until about October first that we could make any real progress in arranging courses. We decided it would probably be best for the first year to try to have courses given during the two weeks immediately preceding this Session, and to have courses offered in the three medical schools where postgraduate work is being done, namely, Harvard Medical School, in Boston, Columbia University, in New York City, and the Graduate School of Medicine of the University of Pennsylvania, in Philadelphia. Seven courses were offered, two in Philadelphia, one in Boston and the other four in New York City. We had a very great response, although our announcements were distributed late. The courses in Philadelphia were oversubscribed, and an adequate number of registrations were received for the course at Harvard and for the course at the New York Post-Graduate Medical School, Columbia University. It was necessary to return excess registrations and checks to about forty who could not be accommodated in the courses at Philadelphia, even though the maximum facilities were somewhat increased. The courses that were finally given were one at Harvard Medical School on General Medicine, which included instruction in all the different phases of General Medicine, there were fifty-five students enrolled in that course; another course in General Medicine, with instructions in different phases of Internal Medicine, was given at the New York Post-Graduate Medical School, Columbia University, where twenty-five students were enrolled; at the University of Pennsylvania, one course was given in Cardiovascular Diseases, under the leadership of Dr. William D. Stroud, with a registration of twenty-four; another in Gastro-Intestinal Diseases, under the leadership of Dr. Henry L. Bockus, with a registration of thirteen students.

"At Columbia University, the course in Neuropsychiatric Factors in Internal Medicine was offered and thirteen bona fide applications were received, but because the number was insufficient, the course was abandoned. Another course at Columbia University on Metabolic Diseases and Digestive Disorders also was abandoned.

"Your Committee feels that this type of instruction, which is a refresher type largely for those in the general field, is popular with the Fellows and Associates, and that the experiment this year was very satisfactory. In spite of the fact that we had a late start, we had a very good showing and tremendous interest was aroused throughout the country. We feel that with this experience, in another year we will be able to get an earlier start and will have things arranged well ahead of time. We believe that the total cost of underwriting the courses, which will later be furnished by the Executive Secretary, will not exceed five hundred dollars, and the price of the course to the Fellows and Associates was kept down to $40.00, whereas ordinarily a considerably higher tuition fee is charged.

"The other phase of the work of the Committee concerns its survey of postgraduate instruction. No definite survey has yet been made. Your Committee has only recently been enlarged to five members and we have felt that the full Committee should get together to discuss and organize a plan to make the survey. You may know that the American College of Surgeons has a committee working on postgraduate instruction. The American Medical Association likewise is undertaking some studies on its own account, and I believe that the American Board of Internal Medicine is also concerned with this general matter. I think that Dr. James D. Bruce could say something more about this work, because he is on the larger committee. The American College of Surgeons, through its Committee, has shown a willingness to coöperate with us in making any studies that we may wish to make. We do not feel at the moment that we should lay down any definite policy as to how candidates should obtain postgraduate training in this country, and we doubt very much whether any definite standards should be set up or that young workers in hospitals should be guided entirely by some philosophical approach through our organization. We are hoping, if it meets with your approval, to extend our discussions with other interested groups, and probably by another year be able to make some recommendations or suggestions which should be of value. The only report that we have, therefore, is concerning the Postgraduate Courses which were given this year, and which we think have been quite successful. We shall specifically inquire about the reactions of all the students who took the courses this year, in order that we may have a better idea of what is desired."

Dr. James D. Bruce supplemented Dr. Kerr's remarks by saying that he hoped that all the agencies studying the problem of postgraduate education would collaborate on all the information that they have gained within two or three years, to be of service to the profession in general.

Dr. O. H. Perry Pepper inquired if the Committee feels it essential that these courses be given in graduate schools. He expressed the opinion that in the future the undergraduate schools would also have to be used. He also expressed the opinion that many men would rather register for courses in cities other than where the meeting is going to be held, because they would already be assured of obtaining much of the best work in that city during the meeting of the College.

Dr. Kerr replied that the Committee has not been able to try its methods out in the undergraduate schools, but that there should be no difficulty in doing so.

President Means read the following communication by Dr. E. L. Tuohy concerning the course in Boston:

> "The Fellows and Associates of the American College of Physicians, who have assembled and taken the Course of Lectures and Demonstrations at Harvard University, desire to express their deep appreciation of the meticulous care with which the physical arrangements have been made, and the zeal and enthusiasm with which the Harvard Medical Faculty members have given us of their time and clinical experience.
>
> "We desire that this heartfelt expression shall be passed on to the Harvard Medical Faculty; and that its brilliant representative, as President of the American College of Physicians, Dr. James H. Means, shall convey to the Regents of the College, our approval of this needful venture of the College into the development of a workable plan of graduate instruction for its members. From this experience at Harvard we bespeak for future meetings of the College, wherever held, the providing of similar Courses for those who keenly desire to fortify their position in Internal Medicine, with an adequate appraisal of current advances in Medicine."

On motion by Dr. Kerr, seconded by Dr. Bruce, and regularly carried, it was

RESOLVED, that an appropriation of $500.00 be made to cover the cost of underwriting the Postgraduate Courses during 1938.

Another resolution was unanimously adopted thanking the Committee on Post-graduate Education and the Executive Secretary for the work accomplished in developing the plan of graduate instruction for members of the College.

Dr. William D. Stroud, as Treasurer of the College, presented the annual report by the Auditor and the financial statements for the year 1937, commenting upon various items of significance in relation to the Endowment Fund and the General Fund. He discussed the present valuation of the securities and referred to a liquidating dividend received from one of the closed depositories in Pittsburgh.

It was regularly moved, seconded and carried that the report be adopted.

Dr. James Alex. Miller, Chairman of the Committee on Finance, presented the following report:

> "The Finance Committee reports that in the face of the present security market, we consider that the value of our funds has held up remarkably well. We wish to express our appreciation of the wise advice we have had from the Girard Trust Company, who was largely responsible for this—the indication of which is shown by the fact that only 7 per cent of all our investments are in common stocks, in which class of investments the largest depreciation has occurred.
>
> "Since the last meeting, we report that we have purchased for the Endowment Fund $1,000.00 North American Edison, 5s, 1957, at 103.25, and for the General Fund, $1,000.00 North American Edison, 5s, 1957, at 103.25. There have been no sales of securities since the last meeting. The Treasurer and the Executive Secretary report that we have free funds which could be invested, amounting in the General Fund to $10,000.00, and in the Endowment Fund to $3,000.00. The Girard Trust Company recommends that these funds be held in cash for the present. However, we are to get further advice from them for the next meeting of the Regents, but the Finance Committee at present is inclined to follow this advice. We are, however, arranging to have further up-to-date advice from the Girard Trust Company about this matter, and we may have recommendations to make at a subsequent meeting of the Regents.
>
> "On recommendation of the Girard Trust Company, the Finance Committee has authorized the Treasurer to sell $5,000.00 City Service, 5s, 1950, and with the proceeds to buy 50 shares of Air Reduction Company.
>
> "The Finance Committee also suggests that when consideration of the Budget for the next year is taken up, that the desirability of having the expenses for the Governors and Regents Dinner, which is now a fixed function immediately preceding the Annual Session, be provided for in the Budget of the College. This would make it possible to make this Dinner meeting particularly directed toward a discussion of the general affairs of the College, and, in the opinion of the Finance Committee, would be a very justifiable and valuable expenditure."

Upon motion seconded and regularly carried, it was

RESOLVED, that the report of the Committee on Finance be accepted and approved.

Adjournment.

Attest: E. R. LOVELAND,
Executive Secretary

MEETING NO. 2

The second meeting of the Board of Regents, during the Twenty-second Annual Session, convened Tuesday, April 5, 1938, at the Waldorf-Astoria Hotel, New York City, with President James H. Means presiding, and with Mr. E. R. Loveland acting as secretary, and with a total of twenty-one Regents present.

Dr. Charles H. Cocke, as Chairman of the Board of Governors, brought to the Board of Regents the following resolution regarding Fellows and Associates delinquent in dues for two years or more, and who, therefore, were at this time subject to being dropped:

RESOLVED, that the Board of Governors recommend to the Board of Regents that the list of delinquent members of two or more years standing be retained on the Roster for a period of three months after this meeting, pending the possibility of some of them being able to pay their delinquent dues in the meantime.

By resolution, the Board of Regents approved of the recommendation of the Board of Governors.

Dr. James Alex. Miller, as Chairman of the Committee on Finance, made a further report for the Committee, recommending that $3,000.00 of the uninvested Endowment Fund be invested in 3,000 Toledo Edison, First 5s, of 1960. The Committee recommended that there be no further action on the investment of $10,000 from the General Fund at this time.

On motion by Dr. Miller, seconded by Dr. Charles H. Cocke, and regularly carried, it was

RESOLVED, that the Treasurer be instructed to purchase 3,000 (par value), Toleda Edison, First Mortgage, 5 per cent, Bond of 1960 for the Endowment Fund account.

Dr. James Alex. Miller, as Chairman of the Committee on Future Policy for the Development of Internal Medicine, read the following report:

> "A communication from Dr. Henry Wallace, of New York City, was received in which he expressed the wish that the American College of Physicians could have equal share in the inspection and classification of hospitals which the American College of Surgeons enjoys. The Committee considered this question, and it is of the opinion that inasmuch as inspection and classification is now done very adequately by the College of Surgeons, and inasmuch as it requires a very large expenditure of money, probably beyond the means of the American College of Physicians, that Dr. Wallace be informed that the Regents of the College do not consider that this is at the present time either a necessary or desirable new activity for the American College of Physicians.
>
> "Inasmuch as the College now has a Committee conferring with a Committee from the American College of Surgeons on other matters, if the Regents think that this matter is important enough to follow up, it is recommended that this question be referred to that Committee.
>
> "Your Committee has also considered a communication from the Finance Committee of the Commission on Graduate Medical Education of which Dr. Willard C. Rappleye is Chairman, in which the Finance Committee states that the Commission desires to make the basis for its support as broad as possible and is authorized to request contributions to the budget of the Commission from the various sponsoring organizations of which the College is one.
>
> "The budget of the Commission as explained amounts to $76,500 to cover a three-year period. Contribution from the College consequently is solicited on a three-year basis. Your Committee thinks that this is an important matter in which the College is vitally interested and recommends to the Regents that they authorize a contribution to the budget of the Commission on Graduate Medical Education a donation of $100.00 each year for three years, being $300.00 in all."

Dr. James D. Bruce moved that the report be accepted, and Dr. Robert A. Cooke seconded the motion. In discussion, Dr. Bruce mentioned that although the amount

of the budget seemed to be considerable, funds were available to the Commission. He explained that the Commission is not an agency of the American Medical Association through its Council on Medical Education, but is organized under the Specialty Boards; that its program has not yet been fully decided upon, although a director has been appointed and a general policy developed; that it proposes to develop also the philosophy of postgraduate education.

The motion before the Board was put to a vote and carried, as follows:

RESOLVED, that the report of the Committee on Future Policy for the Development of Internal Medicine be accepted, and that the Board of Regents authorize a contribution of $100.00 annually, for three years, to the Commission on Graduate Medical Education.

Dr. Maurice C. Pincoffs, Editor, reported on the ANNALS OF INTERNAL MEDICINE. He pointed out that this journal has increased in size and in circulation steadily. In reference to two controversial addresses presented the first day of the Annual Session, the Editor stated that it would be made plain to the readers of the ANNALS that the College had not adopted any sides in these matters whatsoever. He further suggested that at the time of publication of these two articles, which are against, in many particulars, the feeling of the profession as a whole, an editorial should appear in the ANNALS, making it perfectly clear that the College has taken no position in the situation.

Dr. James Alex. Miller expressed his approval of that plan. President Means also said that he was strongly in favor of such a proposal, and Dr. O. H. Perry Pepper suggested that some well-known representative of the other side of the controversy publish its ideas in the same number of the ANNALS. The Editor, however, replied that he thought it would not be well to publish both sides of the question in the same issue, or in issues closely following one another, but that at the next Annual Meeting of the College some individual might voice the other side of the proposition, which in due time would also appear in the ANNALS.

By motion, seconded and regularly carried, the report of the Editor was adopted.

Dr. Maurice C. Pincoffs, Chairman of the Committee on Revolving Loan Funds, reported as follows:

> "The Committee on Revolving Loan Fund can at this time present a report of progress. It has not been possible to complete our recommendations defining the purpose, outlining the machinery, suggesting the sequence of steps and proposing the budget of the Revolving Loan Fund.
>
> "Our definition of the purpose has somewhat enlarged to include assistance not only to those younger physicians who need help in their studies for certification, but also in special instances or perhaps as a later development to those of our own Associates or Fellows who may apply for aid to make possible needed postgraduate study. Some consideration has been given to the problem of the kind of organization which will be necessary to investigate the applicant in the environment in which he is working. It would seem necessary that the Loan Fund have recognized representatives sufficiently interested in the purpose of the Fund, so that they will undertake the not inconsiderable task of investigating the applicant from first-hand sources, of interviewing the applicant personally and of seeing to it that the necessary blanks are filled out and forwarded to the office of the Executive Secretary. In the appointment of such local representatives, the Loan Fund will no doubt be greatly aided by the Governors' and Regents' knowledge of the personnel of the College.
>
> "The completed applications will, no doubt, be subjected to scrutiny by the Executive Secretary and then passed to a central committee analogous to the Credentials Committee.

"Since the books of the Fund and the handling of application forms will in time entail considerable work, a careful study of the effect on our central office force must be made.

"Estimates as to the necessary budget under the various plans as to number of men to be aided are being drawn up in a tentative way by a local Foundation experienced in the work.

"It is hoped that the committee may have the project in form for your final consideration by the fall meeting."

On motion by Dr. James E. Paullin, seconded and regularly carried, the report of the Committee on Revolving Loan Funds was accepted.

Dr. David P. Barr, Chairman of the Committee on Fellowships and Awards, discussed past and present fellowships that have been awarded by the College. He reported that Dr. Myron Prinzmetal, who was the recipient of the Research Fellowship for 1936, had returned to this country, after his work in the laboratory of Sir Thomas Lewis, and is now associated with the University of Southern California. He also reported that Dr. Robert W. Wilkins, one of the 1937 Research Fellows doing work at the National Hospital in London, had written concerning the possibility of obtaining a position when his fellowship has been completed. Dr. Barr emphasized the thought that the College should consider the matter of placement for these Research Fellows after their studies have been completed. Dr. Barr pointed out that but one Research Fellowship has been awarded for 1938. He asked for suggestions about methods of publicizing these fellowships, in order to get more men to apply. The Committee has been, heretofore, sending letters to about two hundred Professors of Medicine and Pediatrics in this country, to members of the Board of Regents and Officers of the College, asking them for the names of promising candidates for these fellowships.

Dr. James Alex. Miller asked about the methods of the National Research Council in obtaining candidates, whereupon Dr. Barr replied that the National Research Council is more generally known, and that they have, naturally, a larger number of candidates. Dr. Pincoffs announced that in the case of the University of Maryland, announcements are posted in the School and Hospital; Dr. Herrick suggested that notices of the College fellowships might be posted along with those of the National Research Council. Dr. Roger I. Lee suggested announcements through the current medical reviews. Dr. Barr explained that the Committee had recommended the award of only one Research Fellowship for 1938 because the other candidates did not have adequate qualifications, or because other candidates would be cared for through the universities from which they came.

On motion by Dr. Roger I. Lee, seconded by Dr. William D. Stroud, and regularly carried, it was

RESOLVED, that the report of the Committee on Fellowships and Awards be accepted and placed on file.

Dr. James H. Means, as Chairman of the Committee on the Annals of Internal Medicine, reported that there had been no meeting of that Committee, and, therefore, there would be no report.

Dr. Walter L. Bierring, Chairman of the American Board of Internal Medicine, reported as follows:

"Mr. Chairman, this is a report of progress. The list of Diplomates, those who are certified without examination, is practically completed, and comprises about fifteen hundred names. Adding to that those who were first selected as members and advisers of the Board, there are now somewhat over seventeen hundred names. There has been difficulty in limiting the time—that is, the expiration of this opportunity for filing applications without examination—to

July 1, 1937, but the Board has taken a firm stand that the lists are closed, realizing that there will be a goodly number who, perhaps, have been omitted for one reason or another, and no doubt some may have been admitted who should not be.

"The Board is encouraged by its recent practical examination, having examined on April 1, 1938, thirty candidates who had previously satisfactorily completed the written examination at the Bellevue Hospital, of which twenty-three were approved and seven will be required to repeat the examination. Thirty-three were examined at the Presbyterian Hospital in New York City on April 2, of which two will be required to repeat and thirty-one will be recommended for the certification.

"Sixty-three were certified by examination during 1937, to which will be added the fifty-four that will be certified in the present examination. Another examination will be held in San Francisco in June, the days preceding the American Medical Association's meeting, for which there are between thirty and forty candidates at the present time. The membership on the Board comprises five representatives from the College. The terms of Drs. O. H. Perry Pepper and William S. Middleton expire, and the President of the College should nominate candidates to fill the vacancies.

"The Board is encouraged by its progress so far, particularly by the new type of candidates that are appearing, who successfully complete the examinations. It is an assurance of the type of internists of the future and possible future Fellows of the College."

Dr. James Alex. Miller moved the acceptance of the report. It was regularly seconded and opened for discussion.

There was general and free discussion of all features in the operation of the American Board of Internal Medicine—its welfare, prestige and future development, following which the resolution before the Board was approved.

Under new business, Dr. Ernest B. Bradley suggested that at the December, 1938 meeting of the Board of Regents the proposition be considered that the College reimburse the official Governors for their round trip railroad and pullman fares to the Annual Sessions.

The Executive Secretary, Mr. Loveland, reported that there would be an increase of approximately $450.00 per annum in the cost of printing the Annals of Internal Medicine, this being beyond present budget provisions. Mr. Loveland expressed the opinion that he thought the increased cost proposed by the printers, the Lancaster Press, Inc., was a fair one, because of generally increasing costs, new labor legislation, etc. On motion by Dr. Piersol, seconded by Dr. Egerton L. Crispin and regularly carried it was

RESOLVED, that the Board of Regents appropriate $225.00 additional to the budget for printing the Annals of Internal Medicine from July 1, 1938, and that the Executive Secretary be authorized to approve the 2½% rebate to the printers beginning with Volume XII, July 1, 1938.

Following the reading of several announcements, the Board of Regents adjourned.

Attest: E. R. LOVELAND,
Executive Secretary

MEETING No. 3

The third meeting of the Board of Regents of the American College of Physicians, during the New York Session, convened at 1:00 p.m., April 8, 1938, at the Waldorf-Astoria Hotel, New York City, with Dr. William J. Kerr, newly inducted President, presiding, Mr. E. R. Loveland acting as secretary and with thirteen Regents present.

Dr. Charles H. Cocke, Chairman of the Board of Governors, reported that that

Board had unanimously adopted a resolution recommending to the Board of Regents its favorable consideration of New Orleans as the meeting place for 1939.

In accordance with provisions of the By-Laws, Dr. William D. Stroud was reëlected Treasurer of the American College of Physicians for 1938–39, and Dr. George Morris Piersol was reëlected Secretary-General for 1938–39.

New committees for 1938–39 were appointed in accordance with regulations of the By-Laws, or supplemental resolutions of the Board of Regents, the personnel of said committees having already been published in the May 1938 issue of this journal.

Mr. E. R. Loveland, Executive Secretary, presented a resolution signed by approximately 150 Fellows, including Dr. James H. Means, the retiring President of the College, concerning the Presidential Address at the Convocation of the College on April 6. After due discussion and consideration, a committee, consisting of Dr. James Alex. Miller, Dr. O. H. Perry Pepper and Dr. David P. Barr, offered the following resolution for inclusion in the Minutes and for release to the press:

> "Unfortunately an impression has been given by the public press that the American College of Physicians is in revolt against the organized medical profession as represented by the American Medical Association.
>
> "This does not correctly reflect the statement of Dr. Means in his presidential address in which he said,
>
> "'It should be as unthinkable for us to have a College policy regarding social, economic, political or scientific aspects of medicine as for one of our universities to take sides in a political campaign. It should also be unthinkable that we should at any time be unwilling to hear both sides of any problem related to the practice of medicine.'
>
> "Nor does the impression given by the press represent any position taken by the membership since there has been no official consideration by the College of the questions involved."

This resolution was regularly adopted.

On motion by Dr. Ernest B. Bradley, seconded and regularly carried, it was

RESOLVED, that the Editor of the ANNALS OF INTERNAL MEDICINE be requested to prepare an editorial embodying the general principles of the above resolution and the preceding discussion.

The next order of business was the selection of the 1939 meeting place, and invitations also for the 1940 meeting place. The Executive Secretary presented an invitation from Boston for 1940. He then presented invitations from Washington, D. C., San Francisco, Cincinnati, St. Paul, Cleveland and New Orleans. Dr. S. Marx White, of Minneapolis, appeared in person to further discuss the invitation from St. Paul. After general discussion of all the invitations and the reading of a telegram from Dr. John H. Musser, New Orleans was unanimously selected by resolution as the place for the 1939 Annual Session.

On motion by Dr. Bradley, seconded by Dr. Piersol and regularly carried, it was

RESOLVED, that the dates for the 1939 meeting be left to the President, the General Chairman and the Executive Secretary.

Dr. John H. Musser was unanimously appointed the General Chairman for the 1939 Annual Session.

Mr. Loveland, as secretary, read the following resolution, supplementing the invitation from New Orleans:

> "Whereas, It has been customary for the American College of Physicians to organize Post-Convention Cruises to various points of the world; and
>
> "Whereas, A Chapter of the College was established and is properly functioning in this Island of Puerto Rico, United States of America; and

"Whereas, The ever increasing medical facilities in this Island will no doubt prove interesting and perhaps profitable, at least in the line of Tropical Medicine, to members of the cruise; and

"Whereas, These cruises prove both beneficial and stimulating to the medical profession of Puerto Rico as a whole; and

"Whereas, The Government of Puerto Rico has undertaken a vast program of tourism and is willing to coöperate fully, through its various agencies, with the College in order to assure a pleasant visit to the Island; now, therefore, be it

"RESOLVED, By this Puerto Rico Chapter of the American College of Physicians to request from the College the pleasure and privilege of organizing, as soon as circumstances permit, a Post-Convention Cruise to the Island of Puerto Rico."

President Kerr suggested that the College thank the Governor and Fellows of Puerto Rico for their invitation, and advise them that said invitation has been taken under consideration.

Dr. Francis M. Pottenger, in accordance with an action of the Board of Regents on April 3, 1938, presented the following resolution in regard to the proposed law against animal experimentation which was before the Committee on Legislation in the State of California, and recommended the following resolution:

"The American College of Physicians is opposed to any type of legislation restrictive to and preventive of properly conducted medical investigation. It therefore declares its opposition to such legal action as is currently proposed in the State of California, which, if adopted, would seriously interfere with the study of diseases of both animals and men."

On motion by Dr. Piersol, seconded by Dr. Bradley and regularly carried, the above resolution was adopted.

It was pointed out that the above resolution opposing anti-vivisection legislation in California, while not a controversial matter in the medical profession, is a matter in which medicine is greatly concerned, and that the College does from time to time put itself on record concerning things which are not necessarily connected with medical economics or medical ethics. President Kerr stated that the universities in California are taking a very active stand against anti-vivisection laws.

Referring to the editorial which he had been instructed to prepare previously in these Minutes, Dr. Pincoffs suggested that said editorial should be passed upon by the Committee on Public Relations and probably by the Editorial Board before it should appear in the Annals.

Dr. O. H. Perry Pepper reported that in connection with the Bicentennial Celebration of the University of Pennsylvania, an effort is being made to have learned societies meet in Philadelphia during the spring of 1940, and expressed the hope that the College may meet in Philadelphia during 1940.

In regard to postgraduate study, President Kerr suggested that the opportunity be extended not only to Fellows and Associates, but also to Licentiates of the American Board of Internal Medicine who desire to keep their interest alive until the time they may be able to qualify for membership in the College.

On motion by Dr. James Alex. Miller, seconded by Dr. James D. Bruce and regularly carried, it was

RESOLVED, that the Committee on Postgraduate Study be instructed to admit to Postgraduate Courses offered by the College those certified by examination by the American Board of Internal Medicine; preference, however, to be given to the applications of Fellows and Associates of the College.

Adjournment:

Attest: E. R. LOVELAND,
Secretary

ANNALS OF INTERNAL MEDICINE

PUBLISHED BY

The American College of Physicians

VOL. 11 (O.S., Vol. XVI) JUNE, 1938 NUMBER 12

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Acceptance for mailing at a special rate of postage provided for in the Act of February 28, 1925, embodied in paragraph 4, section 538, P. L. & R., authorized October 7, 1936

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ANNALS OF INTERNAL MEDICINE

OFFICIAL PERIODICAL OF THE AMERICAN COLLEGE OF PHYSICIANS

Place of Publication—Prince and Lemon Sts., Lancaster, Pa.

Editorial Office—University Hospital, Baltimore, Md.

Executive Office—4200 Pine Street, Philadelphia, Pa.

THE ANNALS OF INTERNAL MEDICINE is published by the American College of Physicians. The contents consist of contributions in the field of internal medicine, editorials, book reviews, and a section devoted to the affairs of the College.

MANUSCRIPTS. All correspondence relating to the publication of papers and all books and monographs for review should be addressed to the editor. No manuscripts will be accepted without his consideration. Bibliographic references are to conform to the following style:

4. DOE, J. E.: What I know about it, Jr. Am. Med. Assoc., 1931, xcvi, 2006-2008.

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